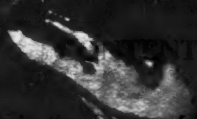
VOL. V. No. 4 OCTOBER, 1943

BRITISH HEART JOURNAL

EDITORS
MAURICE CAMPBELL
D. EVAN BEDFORD

APPOINTED BY
THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND



CONTENTS

PAGE

Auricular Fibrillation late in the Course of Diphtheria. By A. M. G. CAMPBELL, PAUL C. GIBSON, and C. R. T. LANE 183

Complete Auriculo-Ventricular Dissociation with High Ventricular Rate in Paroxysmal Tachycardia. By CLIFFORD G. PARSONS . 187

Persistent Truncus Arteriosus. By ROBERT MARSHALL . . . 194

Coarctation of the Aorta, Double Mitral A-V Orifice, and Leaking Cerebral Aneurysm. By J. N. P. DAVIES and J. A. FISHER . . 197

Triple Heart Rhythm. By WILLIAM EVANS 205

Treatment of Subacute Infective Endocarditis with Heparin and Chemotherapy. By W. TREVOR COCKS and A. BRIAN TAYLOR . . 229

Proceedings of the Cardiac Society of Great Britain and Ireland . 238

Index 243

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

PUBLISHED QUARTERLY SUBSCRIPTION 25/- PER ANNUM. U.S.A. $6.00

EDITORIAL BOARD

APPOINTED BY
THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

CRICHTON BRAMWELL, MANCHESTER
BOYD CAMPBELL, BELFAST
JOHN COWAN, GLASGOW
FRANCIS R. FRASER, LONDON
A. C. GIBSON, OXFORD
JOHN HAY, LIVERPOOL
SIR THOMAS LEWIS, LONDON
HENRY MOORE, DUBLIN
JOHN PARKINSON, LONDON
W. T. RITCHIE, EDINBURGH
K. D. WILKINSON, BIRMINGHAM
EDITOR OF BRITISH MEDICAL JOURNAL

NOTICE TO CONTRIBUTORS

Contributors, who do not know the Editor's present address, should send papers to:

Maurice Campbell,
B.M.A. House,
Tavistock Square,
London, W.C.1.

Papers dealing with problems of the heart or of the circulation are accepted on the understanding that they have not been and will not be published in whole or in part in any other journal.

Papers sent for publication must be typed as concisely as possible with double line spacing and a good margin. They must be accompanied by a short summary. Manuscripts should be carefully revised as alterations in print are costly and apart from slight corrections will be charged to the contributor. The author whose name comes first will receive one proof in page.

Illustrations must be ready for reproduction, except that on figures lettering which is written in pencil will be replaced by printer's type without charge. The lettering on electrocardiograms should be done in ink and they should be mounted ready for reproduction.

Where there are many electrocardiograms, only a few complexes should be shown, so that several can be mounted together, and their total width should not exceed 4½ inches, or at the most 5 inches, unless they can be reduced in size.

References to papers in the text should be made by the name of the author and the year, with or without brackets. At the end of the paper they should be arranged alphabetically as follows, according to the Harvard system.

Author's name, Initials, Year, Journal (abbreviated according to the World List of Scientific Periodicals), Volume number, Page number, e.g.:

Cowan, J. (1928). *Quart. J. Med.*, 22, 237.

Fifty reprints will be given to the author or divided among the authors on giving notice when the proof is returned. Further reprints, if desired, may be obtained from the Secretary of the Journal Board, B.M.A. House, Tavistock Square, London, W.C.1, to whom all business communications should be addressed.

The subscription, 25/- per annum (20/- to members of the B.M.A.), is payable to the British Medical Association. Applications for advertisement space should be made to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1.

AURICULAR FIBRILLATION LATE IN THE COURSE OF DIPHTHERIA

BY

A. M. G. CAMPBELL, PAUL C. GIBSON, AND C. R. T. LANE

Received June 21, 1943

Auricular fibrillation has been recorded as occurring in diphtheria during two distinct phases of the disease. During the acute phase, when the heart is gravely damaged, it may be incidental to progressive failure, and, much more rarely, it may be a later manifestation without any other sign of myocardial damage. It is an example of this second type that we record here. It may be some measure of the rarity of the association of auricular fibrillation with diphtheria that of three standard American text-books of cardiology, Fishberg (1940), Pardee (1941), and White (1937), only one (Fishberg) mentions it, and that only in a simple statement that in diphtheria the pulse may be irregular as the result of extrasystoles, auricular fibrillation, and other disturbances of rhythm. Burkhardt *et al.* (1938) found no case of auricular fibrillation in 140 adults with diphtheria, examined electrocardiographically every second or third day of their stay in hospital. We cannot accept the statement of Neubauer (1942) that 2 of his 100 cases of diphtheria with heart lesions showed transient auricular fibrillation, because, in the only examples he records (his Fig. 14), the rhythm of one is regular in lead III and the irregularity in lead II could be extrasystolic, and in the other (his Fig. 15), who had a severe heart lesion, it cannot be auricular fibrillation for the ventricular rhythm is in fact regular. Parkinson (1915) recorded the case of a youth, aged 22, who was admitted to an isolation hospital on November 8, 1913, suffering from pharyngeal diphtheria. On November 30, he developed heart block, followed, on December 11, by auricular fibrillation, without any other evidence of myocardial damage. He was discharged from hospital on January 17, 1914, still fibrillating. Seen finally in June, he was still without symptoms and could walk seven miles without dyspnœa, but he was still fibrillating; how much longer it lasted is unknown. It was learnt that he was accepted for Army service in India in 1914, that he remained on active service until 1919, when he came home on leave after having had malaria; he was then in the best of health but six weeks later he developed pneumonia and died. This is the only case record similar to ours that we have found, but, owing to war conditions, we have been unable to make an exhaustive search. The occurrence of fibrillation as an isolated manifestation of myocardial damage in diphtheria is sufficiently rare to justify this case record.

Case Notes

K.S.L., a dentist, aged 39, was serving in the R.A.F.V.R.

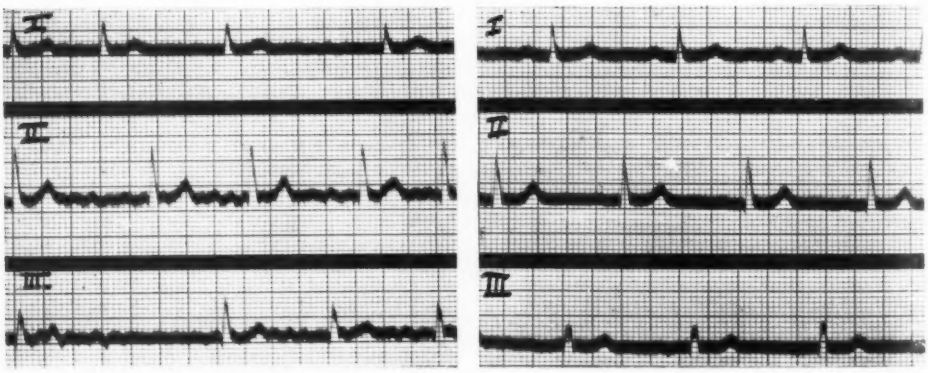
His mother had died of a stroke following hypertension. His father, aged 70, had just recovered from an attack of hypertensive congestive failure. His brother had been confined to bed for two years, following what was stated to be a cardiac complication of measles.

He gave no history of any illness other than complaints of childhood. He had never had rheumatism or chorea. He had always been fit and well; a keen cyclist, he had cycled as much as 140 miles in a day.

On October 6, 1942, he began to feel ill with a sore throat. He did not report sick until two days later, when a diagnosis of follicular tonsillitis was made and he was sent to bed. On October 12, he returned to duty, not feeling unduly ill but rather weak. In retrospect, he remembered seeing, on the first day of his illness, a greyish-white membrane on his throat, which disappeared after one day, leaving a red inflamed area. After a few days he felt much better and cycled 40 miles without undue fatigue.

On October 19 he began to get regurgitation of food through his nose, but, otherwise, felt well and continued at duty. He did not report sick until November 10, when the medical officer realized what was the matter; he was admitted to Torquay Isolation Hospital on the same day. On November 20 he noticed the sudden onset of tachycardia and irregularity of the pulse. It was considered that this was due to extrasystoles and, in view of the likelihood of mycardial damage, he was ordered complete rest. About this time he also noticed tingling of his hands and feet. About December 10 the palatal paresis began to improve and he was allowed to get up gradually. He was discharged to sick leave on December 19. Whilst he was in hospital three throat swabs were taken, but all were negative for *K.L.B.*; no serum was given.

Whilst on sick leave he led a quiet life, walking short distances only. He felt reasonably well but was easily tired by quite mild exertion. Palpitation was conspicuous, occurring both at rest and on exertion, but he was not breathless. He also noticed an unpleasant tingling in his feet when walking about. On resuming duty, on February 23, 1943, he was referred to one of us (C.R.T.L.). The apex beat was displaced about half an inch to the left, and he was fibrillating, but without pulse deficit. The heart sounds were normal and the blood pressure approximately 140/80. There was some hypoalgesia over the soles of the feet and some loss of deep pain sense in the legs. Fibrillation was confirmed (P.C.G.; Fig. 1 A). He was trans-

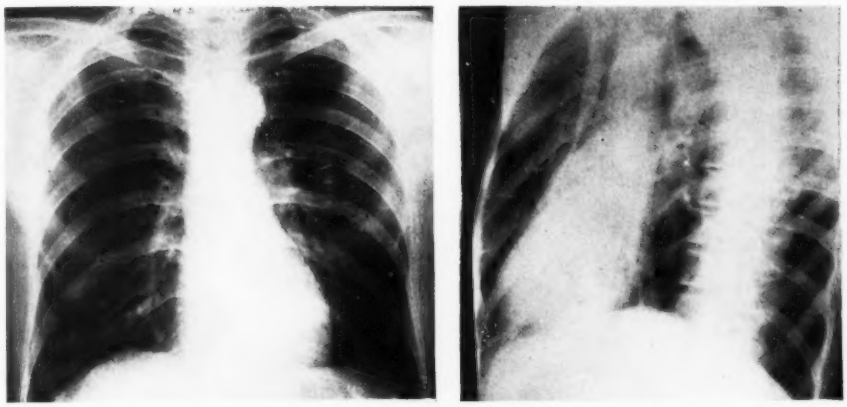


A B

FIG. 1.—(A) Electrocardiogram taken 24/2/43, showing auricular fibrillation. Rate about 80.
(B) Electrocardiogram taken 23/4/43, showing normal rhythm. Rate 68.

ferred to an R.A.F. Hospital, where a radiogram showed no enlargement, but his blood pressure was recorded as approximately 140/100. Quinidine, 5 grains t.i.d., was started on March 5, and after he had had 15 grains the pulse became regular. On April 19 he returned to duty feeling perfectly well. On that day he was seen by A.M.G.C., who found that his nervous system was normal, except for some weakness and displacement of the uvula to the right and diminished vibration sense in both legs. He gave an excellent history and, on being complimented on this, said he had been interested in his illness even to the point of introspection; only now did he refrain from taking his pulse every hour. The second electro-

cardiogram (Fig. 1 B) showed no abnormality except small P waves. The heart rate was 68. The apex beat was in the fifth space, four and a half inches from the mid-sternal line, and was rather forcible. The blood pressure, sitting and recumbent, taken three times in each position, was consistently 145/95. The radial arteries did not seem thickened. The fundi



A B

FIG. 2.—(A) Teleradiogram showing normal size of the heart.
(B) Teleradiogram in right anterior (II) oblique position.

were normal. Later, radiograms (Fig. 2) showed no enlargement of auricles or ventricles. The urine was examined and found to be normal, chemically and microscopically.

COMMENTARY

The association of peripheral neuritis with myocardial damage in diphtheria is well known. Burkhardt *et al.* (1938) found the incidence of peripheral nerve palsies very high in those cases of diphtheria that showed electrocardiographic changes. From another angle, Walshe (1941) stated that in polyneuritis there is always some myocardial damage. Our case conforms with these views and supports the suggestion that it is desirable to seek for cardiographic changes in all cases of diphtheria, irrespective of severity, that have peripheral nerve lesions.

There is a possibility, emphasized by Geoffrey Bourne (1940) that some chronic local change in the heart, the commonest probably being vascular disease, may account for incomplete recovery after diphtheritic myocarditis. In our case there was a family history of arteriosclerosis and our patient himself showed some evidence of this, though only if his diastolic pressure is accepted as such.

Another feature of interest is the long period that elapsed after the onset of diphtheria before auricular fibrillation was established. This was also found in Parkinson's patient. In both cases fibrillation occurred during convalescence.

SUMMARY

In a man of 39 years old, we record auricular fibrillation, which arose during his convalescence from diphtheria. It lasted for 112 days, when it was stopped by quinidine. Except for his palpitation, it was unaccompanied by any symptoms referable to the cardiovascular system. It was associated with multiple peripheral neuritis, which preceded its onset by 32 days. There was a family history of arteriosclerosis and some slight evidence of this in the patient himself.

We are indebted to the Medical Director General, R.N., and the Director General of Medical Services, R.A.F., for permission to publish this paper, to Wing Commander A. Nelson-Jones for supplying notes on treatment given at the R.A.F. hospital, and to Surgeon Commander A. R. Thomas, R.N.V.R., for the radiographic investigation, and we particularly wish to thank Dr. John Parkinson for his advice and assistance.

REFERENCES

Bourne, G. (1940). *Lancet*, **2**, 96.
Burkhardt, E. A., Eggleston, C., and Smith, L. W. (1938). *Amer. J. med. Sci.*, **195**, 301.
Fishberg, A. M. (1940). *Heart Failure*, 2nd ed., 589. London.
Neubauer, C. (1942). *Brit. med. J.*, **2**, 91.
Pardee, H. E. B. (1942). *Clinical Aspects of the Electrocardiogram*, 4th ed. London.
Parkinson, J. (1915). *Heart*, **6**, 13.
Walshe, F. M. R. (1941). *Lancet*, **1**, 33.
White, P. D. (1938). *Heart Disease*, 2nd ed. New York.

COMPLETE AURICULO-VENTRICULAR DISSOCIATION WITH HIGH VENTRICULAR RATE IN PAROXYSMAL TACHYCARDIA

BY

CLIFFORD G. PARSONS

Received July 19, 1943

The ventricular rate in auriculo-ventricular dissociation is commonly less than 60, and in 1923 Hewlett was able to find only 14 recorded instances in which this rate was exceeded. Most of these patients were under the influence of digitalis and all but one of the remainder had organic heart disease; the exception was a woman whose dissociation developed after tonsillectomy (White, 1916). In Hewlett's own case the P–R interval was considerably prolonged, and during attacks of dissociation the ventricles usually, although not invariably, beat more rapidly than the auricles; most reported examples which he quotes had auricular rates exceeding the ventricular. His observations led him to conclude that the occurrence of dissociation is favoured, on the one hand by the presence of partial A-V block or by the administration of digitalis, and on the other by factors tending either to decrease the auricular or to increase the ventricular rate. White's patient, for example, having recovered from a spontaneous attack of dissociation, would still develop the abnormal rhythm if the carotid sinuses were stimulated, the auricles slowing until the A-V node escaped. Hewlett felt that the rapid ventricular rate in his own patient, together with the conspicuous effect on the rhythm of changing vagal tone, were evidence that the pacemaker lay in the A-V node.

Cowan (1939) reviewed ten cases of dissociation and of these only two had sound hearts, both having a slow ventricular rhythm; all ten had ventricles beating either at the same rate or rather faster than the auricles. This point is emphasized by Katz (1941) for distinguishing between dissociation, which he regards as a functional condition, and heart block, which is frequently due to organic disturbance. " In dissociation the rate of the ventricles is equal to or faster than that of the auricles, while in A-V block, with rare exceptions, the reverse is true."

Barker and his colleagues (1943), in an interesting paper, discuss the occurrence of A-V block in paroxysmal auricular tachycardia. After reviewing 17 previously reported cases they describe 18 of their own and compare the condition with auricular flutter, pointing out, amongst other features, that carotid sinus pressure slows the ventricles without influencing the auricular rate, and usually fails to arrest the attack. The degree of block encountered ranged from partial block with occasional dropped beats, through 2 : 1 and higher grades of A–V block, to two examples of complete heart block. These last two patients had regular ventricular rates of 84 and 26 respectively; one, a woman aged 26, had organic heart disease, and the other was a man of 70, reported by Singer and Winterberg (1922).

A somewhat different abnormality of rhythm was described by Barker (1924), who reported a case of paroxysmal auricular tachycardia in which an attack was disturbed by a brief phase of ventricular tachycardia. The ventricular contractions were slightly irregular and no auricular complexes could be identified. The patient had had attacks of palpitations for 36 years and her heart was otherwise sound.

The report which follows concerns a patient subject to attacks of paroxysmal auricular tachycardia. She had no evidence of organic heart disease and had had no drugs. A spontaneous, short-lived attack in which auricles and ventricles beat quite independently, each at a rate well in excess of 100, was recorded during her first appearance at hospital.

Case Report and Electrocardiograms

A woman of 29 attended hospital in November 1942, complaining of attacks of palpitation which she had had for 7 years. The paroxysms occurred two or three times a day, always started and ended abruptly, lasted from ten minutes to two hours, and were precipitated especially by emotional upsets. She was a well-built, healthy woman with an apparently normal heart. There were no signs of hyperthyroidism and the only focus of infection lay in some doubtful teeth which were removed later without influencing her attacks. Blood count, sedimentation rate, and X-ray of chest were all normal.

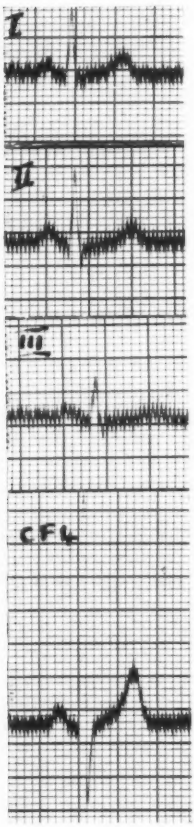


Fig. 1.—Sinus rhythm.

She was not unduly distressed during an attack of tachycardia; her pulse rate was 136, quite regular, and uninfluenced, clinically, by exercise or carotid sinus pressure. A triple venous pulse wave was visible at the root of the neck and the heart sounds were normal apart from their rapidity.

Electrocardiograms taken during sinus rhythm (Fig. 1) are normal in every respect. The P–R interval has been measured on numerous occasions and varies between 0·14 and 0·16 sec. Many records have been taken in the course of her paroxysms of tachycardia and practically no variation has been seen. The attack invariably starts with a premature P wave lying early in the descending limb of the preceding T; during the paroxysm P and T waves are superimposed and the sequence ends with a compensatory pause before the resumption of sinus rhythm (Fig. 2). The heart rate in these episodes is 136 and the P–R interval (which in this and subsequent records is measured from the summit of P to the summit of R) is slightly longer than in sinus rhythm, i.e. 0·16–0·18 sec.

Occasional isolated extrasystoles, which resemble the first beat of the tachycardia, have been observed and from the appearance of these complexes it would seem that the excitable focus must lie either in, or very close to, the S-A node.

Fig. 3 shows the first cardiogram obtained from the patient. In the limb leads the auricles are beating regularly at a rate of 152 whilst the ventricules have assumed an independent rhythm which varies between 113 and 136. The P waves in leads I and III are rather larger than those in records of sinus rhythm, and this, combined with the fact that their rate is greater than that in paroxysms of auricular tachycardia, may mean that a kind of flutter has developed. The QRS complexes are of supraventricular type and do not differ materially from those seen in other tracings, but the T waves are inconspicuous. The form and rate of the ventricular waves suggest that they arise in or near the A-V node. In CF_4 the rhythm is much the same as in the limb leads, but the auricular rate is a little slower and there may conceivably be conduction from auricles to ventricles, anyway after the first, seventh, and eleventh auricular contractions. CF_1, taken a few seconds later, opens with what seems to be the last beat of a paroxysm of auricular tachycardia; this is followed by two sinus beats, a short paroxysm of auricular tachycardia and finally by normal sinus rhythm.

The patient would not come into hospital for investigation and the following observations were therefore carried out in the out-patient department. They were kindly made for me by Dr. D. R. Humphreys working in Professor K. D. Wilkinson's clinic at the Queen Elizabeth Hospital, Birmingham.

Measurements reproduced in the various figures which follow are derived from naked eye examination without the aid of a comparator. They are therefore not strictly accurate but may serve to

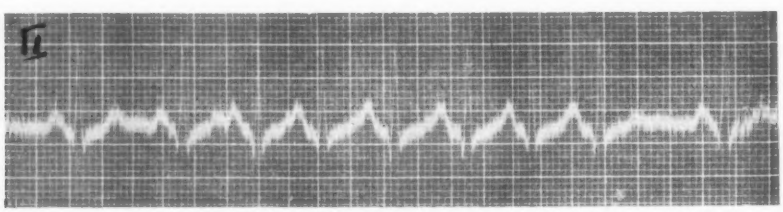


Fig. 2.—Onset and ending of a paroxysm of auricular tachycardia.

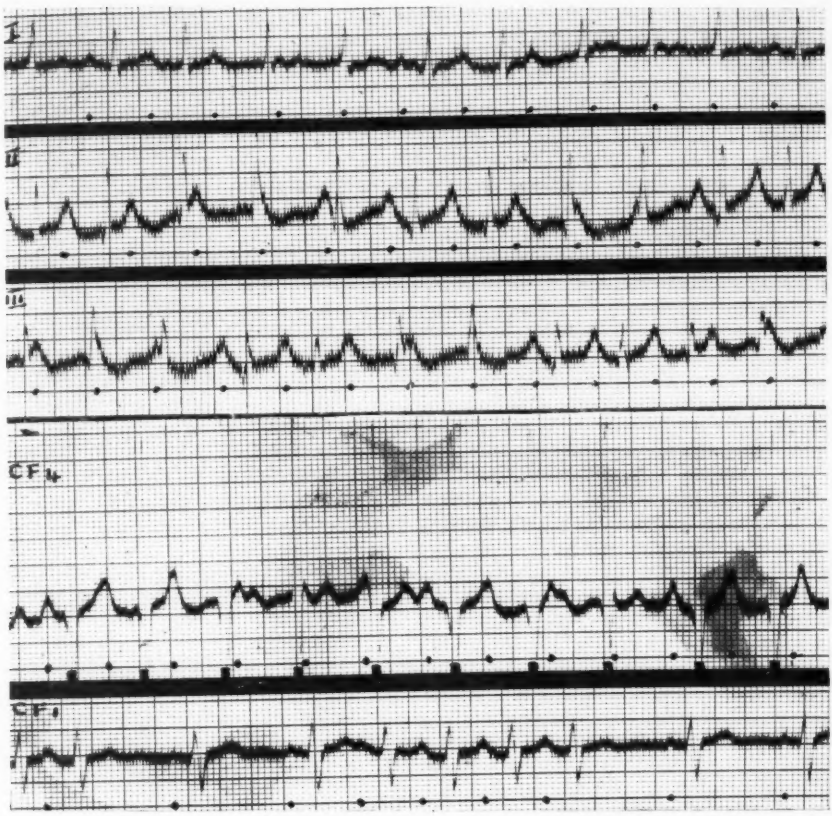


FIG. 3.—Cardiogram showing complete dissociation between auricles (marked with dots) and ventricles, in leads I, II, III, and probably in CF_4. CF_1 shows paroxysms of tachycardia and normal sinus beats.

emphasize the points brought out by the records. Exercise had absolutely no effect on the rate or form of a paroxysm of auricular tachycardia. Pressure on the left carotid sinus or on both sinuses simultaneously led to the resumption of sinus rhythm for a single beat (Fig. 4). The auricular rate continues practically unchanged whilst the ventricles beat more slowly. The last visible P wave before the sinus contraction is smaller than its predecessors, but it falls in front of, instead of on, a T wave and it does not differ materially from the P of the sinus beat. The next P wave is lost; it is perhaps directly superimposed on the QRS as the voltage of that complex is a little greater than the average. The T wave in the ventricular beat resembles that of the preceding complex, being much less conspicuous than its successor. The S–T interval is slightly depressed.

Lewis (1925) has pointed out that stimulation of the left carotid sinus will often decrease the speed of conduction from auricle to ventricle. If it is assumed that the missing auricular wave in Fig. 4 is buried in the ventricular beat, this may be an example of the Wenckebach phenomenon. The length of successive P–R intervals, measuring 0·16 sec. in the early beats, increases to 0·18, 0·30 and 0·39 before a beat is dropped and sinus rhythm is restored. The successive increments are therefore 0·02, 0·12 and 0·09, the first of which might perhaps be ignored. Further discussion of this subject follows later.

Five minutes after the sinus compression experiment, two minims of adrenalin (1 : 1000) were injected intravenously, in an attempt to stimulate the sympathetic. The patient became pale, shaky and apprehensive, with rather a feeble pulse. At the same time some interesting changes developed in the electrocardiograms. Fig. 5 is a section of the tracing taken immediately after injection. It shows two runs of tachycardia separated by a sinus contraction. The auricles continue to contract regularly at the paroxysmal rate of 136, whilst the ventricular rate slows. The last visible P wave in both of the abnormal sequences is small, but this can be explained by the fact that they are not directly superimposed on T waves (a small T is visible in the two beats before the sinus contraction). It is possible

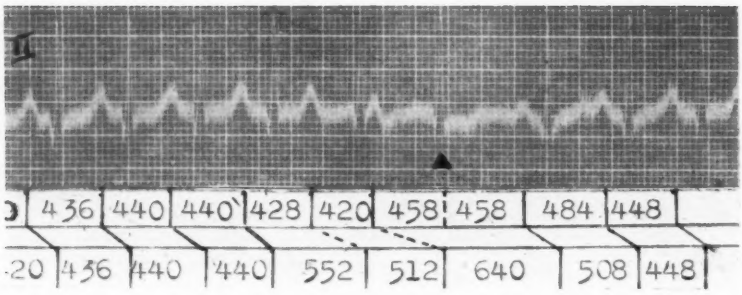


FIG. 4.—Effect of compression of the left carotid sinus during an attack of paroxysmal tachycardia.

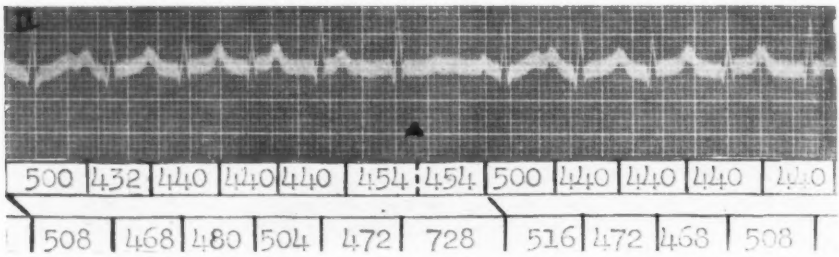


FIG. 5.—Paroxysm of tachycardia immediately after administration of adrenalin.

that a P wave falls on the final QRS of the first sequence, but if this is so the auricular contraction must be somewhat premature. The QRS waves in this tracing vary considerably in voltage but are obviously smaller than the average throughout. In other respects the record is not unlike an exaggerated version of that obtained by carotid sinus pressure.

Half a minute afterwards (Fig. 6), the same effect is still present, with the auricles beating regularly

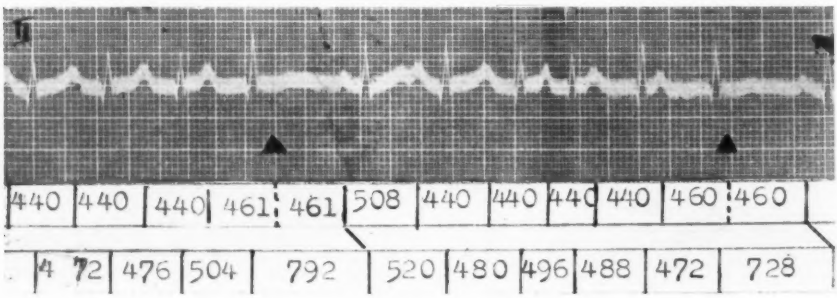


FIG. 6.—Approximately half a minute after adrenalin.

at a rate of 136 and the ventricles lagging behind. The last P seen in the first sequence does not differ from those which go before it; presumably it is superimposed on a T wave. In the second sequence the final P is of lower voltage, but it lies just before a small T wave. It should be noted that the third P wave of this sequence differs in shape from the others because of a momentary sticking of the film in the camera. A recurrence of this mechanical defect mars several parts of the continuous record taken throughout this experiment and makes measurements impossible in some places.

The section of film shown in Fig. 7 was taken about a minute after the exhibition of adrenalin and again demonstrates essentially the same features. By the end of the second minute (Fig. 8) the effect of the drug is beginning to wear off, but the same tendency is still recognizable, the auricles continuing at their old rate of 136 and the ventricles beating rather more slowly. The shape and size of P waves is to all intents and purposes constant and for a P wave to be superimposed on the QRS before the sinus beat, considerable prematurity would be necessary.

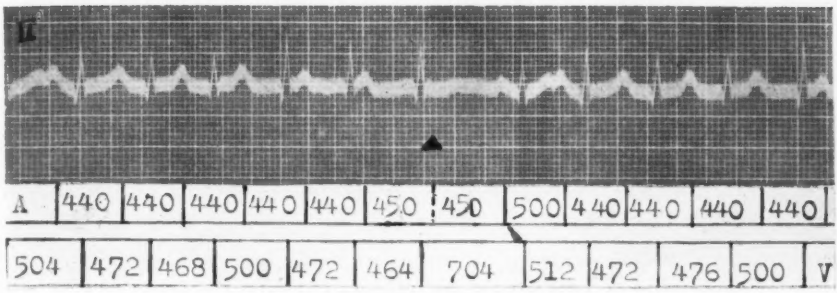


FIG. 7.—One minute after adrenalin.

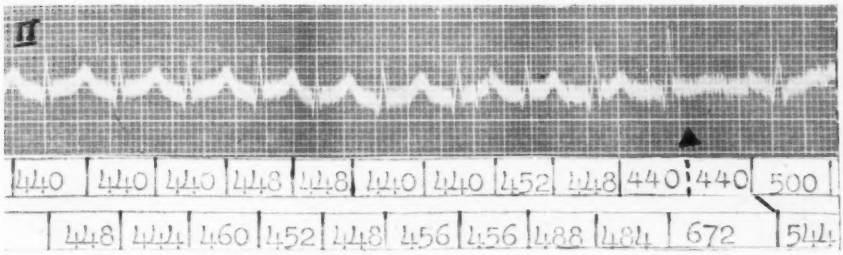


FIG. 8.—Two minutes after adrenalin.

Three quarters of an hour after giving the adrenalin an attempt was made to lower vagal tone by the injection of atropine (gr. 1/100) subcutaneously. Unfortunately the continuous film ran out at this point, but Fig. 9 (upper half) shows the state of affairs in lead I, 15 minutes later. The auricles

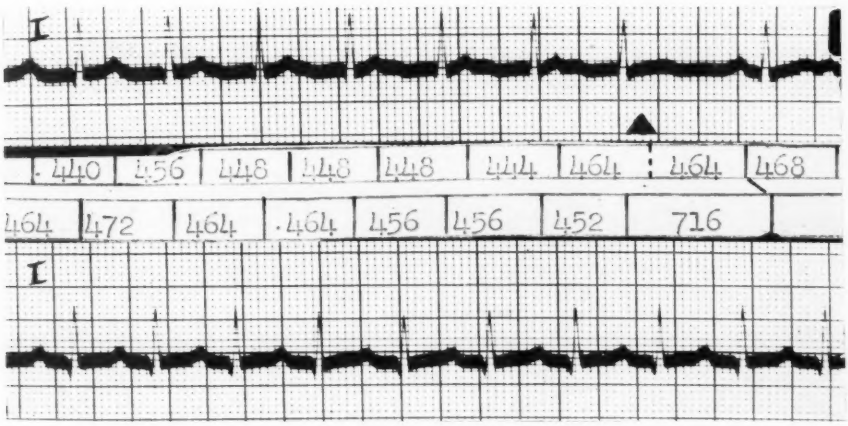


FIG. 9.—Twenty minutes after atropine.

are beating a little more slowly than in previous tracings but the ventricles are still slower than the auricles. The general features are the same as those already described after the injection of adrenalin, but in this film P and T waves are more readily distinguished. The QRS preceding the sinus contraction is not greater in voltage than the other waves of the curve and it seems unlikely that a P wave is incorporated in it. The sinus beat is followed by a premature P, lying in the descending limb of T, and almost certainly marks the initiation of the paroxysm of auricular tachycardia which is shown in the lower tracing, taken a few seconds later. The rate in this paroxysm is 141.

Discussion

Adrenalin, atropine, and probably carotid sinus pressure have all produced the same effect on a paroxysm of tachycardia. Lewis (1925) states that adrenalin, besides stimulating the sympathetic nerve endings, also acts directly on the vagal nerve centres in the medulla. Cushny (1936) agrees that the vagal centres may be stimulated, although he argues that it is not a direct action but a reflex stimulation following a rise of blood pressure. He points out too, as other writers have done, that atropine given in small amounts may activate instead of depressing the tenth nerve. It is probable, therefore, that the similar effects of all three experiments is due in each case to stimulation of the vagus.

It has already been observed that vagal stimulation may diminish the speed of conduction from auricles to ventricles. The Wenckebach phenomenon is characterized by three main features. The P–R interval progressively increases in length with each beat but the degree of lengthening decreases in successive complexes. Consequently the R–R intervals tend to become shorter and shorter until a beat is dropped. During the sequence auricular complexes are followed by ventricular complexes until the ventricle defaults, leaving an isolated P wave before the next sinus beat. Campbell (1943) has demonstrated, however, that the rule of P–R increments is not invariable and that occasionally the increase of the third interval over the second is greater than that of the second over the first.

Allowing both for Campbell's findings and for the fact that measurements taken from the tracings are not strictly accurate, it remains difficult to reconcile the figures (summarized in the accompanying table) with a diagnosis of partial heart block. Moreover in some of the cardiograms the R–R intervals tend to increase instead of diminishing with each successive beat.

Table Showing P–R Intervals and Increments Measured in Thousandths of a Second

Figure	P–R interval	Increment
4	160 ?180 308 392	?20 128 84
6a	180 208 248 308	28 40 60
6b	160 180 220 280 328 360	20 40 60 48 32
8	184 200 208 220 210 200 220	16 8 12 −10 −10 20
	240 260 308	20 20 48

The argument that partial heart block is responsible for the abnormal rhythm shown in Fig. 4–9 is in any case based on an assumption that seems quite unwarranted. It has been pointed out that in partial block the last wave before the sinus beat should be auricular. In none of the tracings is this final P wave visible and it has to be assumed therefore that it is superimposed on a QRS complex. This necessitates the further assumption that the quite regular auricular rhythm is broken, for in practically every instance the P wave would have to be slightly premature to fall directly on the QRS. Black triangles on the figures show the points at which the P waves would have fallen if the auricles had continued at their original rate. It is unbelievable that a premature P wave could fall with such exactness on a QRS on so many occasions. Consequently it is most improbable that this is an example of partial heart block with dropped beats, and if the condition is due to such a defect it is of most unusual type.

The changing shape of the P waves may suggest that there is a shift of the pacemaker towards the A-V node, but the alteration in size is also explicable by the relationship of the P and T waves, P being smaller only when the two fail to coincide. This is made the more probable explanation because in some of the tracings (Fig. 6 and 8) there is no change in the size of the P wave. The progressive lengthening of the P–R interval is a further argument against this diagnosis.

A third, and more probable, interpretation of the abnormal rhythm produced by vagal excitation is that there are short runs of complete A-V dissociation linked by isolated sinus beats. This would be in keeping with the spontaneous attack of dissociation illustrated in Fig. 3, especially if it is allowed that there are occasional sinus beats in CF_4. The development of the independent auricular and ventricular rhythms must be based on factors quite different from those which caused dissociation in White's (1916) case, or those mentioned by Hewlett (1923), for in the present instance the auricular rate continues unchanged and it is the ventricles that beat more slowly. It is likely that the auricles are driven by an excitable focus lying in or near the S-A node, a focus which is usually responsible for paroxysms of auricular tachycardia. In certain circumstances a barrier develops in the region of the A-V node, preventing the passage of impulses to the bundle. When this barrier is present the ventricular rhythm is probably governed by a second pacemaker lying in the neighbourhood of the A-V node. This pacemaker, having been sensitized to a high speed of activity by a paroxysm of auricular tachycardia, continues to send out impulses at a rapid rate, and so there develops a simultaneous auricular and nodal tachycardia.

Some light is thrown on the nature of the A-V nodal barrier by the effect of vagal stimulation during attacks of auricular tachycardia. The dissociation produced is then intermittent, with a sinus beat separating one period of block from the next. The sinus beat is always preceded by a dropped auricular beat. This suggests that the relatively long period of auricular inactivity allows sufficient recovery in the area around the A-V node for the next auricular impulse to follow its normal path to the ventricle. The passage of this solitary contraction wave again disarranges the mechanism and leaves a barrier which persists until the auricles once more default. The defect probably results from an abnormally long refractory period in the area concerned and is presumably related to the mechanism responsible for the Wenckebach phenomenon.

If the rhythm in all the records is in fact due to dissociation, it becomes difficult to decide at what point, following carotid sinus pressure (Fig. 4), conduction gives way to the two independent rhythms. It happens that this is the one electrocardiogram in which the Wenckebach phenomenon may be present, for it is easy to believe that the missing P is superimposed on a QRS. If, however, dissociation is present it probably develops at the fifth beat, where there is a sudden lagging of the ventricle. It will be noted that, as observed by Barker and his colleagues (1943), carotid sinus pressure fails to arrest the attack, but slows the ventricles.

Cardiograms not unlike the record in Fig. 3 were obtained from three of the patients described in Barker's paper (Fig. 7A, 8B, and 11B). These are considered to be examples of partial heart block, but the mechanism of impaired conduction is not discussed. The irregular rhythm of the ventricles is presumably ascribed to prolonged conduction from auricles to ventricles, but the variations in the P–R intervals are considerable and in the short illustrative tracings follow no obvious pattern, though such a pattern may perhaps be apparent in longer records. As far as can be seen the block is not of the Wenckebach type and is probably related to the mechanism described above. In this connection it is interesting that temporary nodal rhythm was observed in two of these cases. All three patients were receiving digitalis; two had organic heart disease and the third had an enlarged heart and, during attacks of tachycardia, a high blood pressure. The auricular rates in the illustrative records were 212, 188, and 167 with corresponding ventricular rates of 165, 112, and 131.

One other patient relevant to the discussion (Case 9) was a woman suffering from chronic rheumatic heart disease who, when under the influence of digitalis, developed tachycardia with partial block. Exercise increased the auricular rate slightly and "... the ventricles responded to each auricular beat for a short time, then became slower and irregular and finally displayed a long period of near standstill, interrupted by idiopathic ventricular beats. ..." These idiopathic complexes are similar in structure to the complexes throughout the record, suggesting a point of origin close to the A-V node. This makes it clear that, in some cases of paroxysmal tachycardia, the auricular impulses may fail partly or completely to stimulate the ventricles, and that there is a tendency for the ventricles to be controlled by a pacemaker lying in or near the A-V node, the impulses from which are not necessarily regular.

On account of wartime conditions a thorough search of the literature has been impossible, but a limited review has revealed no other case in which the particular form of dissociation here described has developed in a patient without organic heart disease and not under the influence of digitalis.

SUMMARY

A case of paroxysmal auricular tachycardia is described, in which there developed a spontaneous attack of A-V dissociation, with high auricular and ventricular rates amounting to a double tachycardia. The condition could be partly reproduced during attacks of auricular tachycardia by atropine, adrenalin, and carotid sinus pressure. The patient's heart was otherwise normal and no drugs had been given. It is suggested that the condition is due to a form of heart block the mechanism of which is allied to, but not identical with, the Wenckebach phenomenon.

REFERENCES

Barker, P. S. (1924). *Heart*, **11**, 67.
Barker, P. S., Wilson, N. W., Johnston, F. D., and Wishart, S. W. (1943). *Amer. Heart J.*, **25**, 765.
Campbell, M. (1943). *Brit. Heart J.*, **5**, 55.
Cowan, J. (1939). *Ibid.*, **1**, 3.
Cushny, A. R. (1936). *Textbook of Pharmocology and Therapeutics*. Revised by Edmunds, C. W., and Gunn, J. A. Churchill, London.
Hewlett, A. W. (1923). *Heart*, **10**, 9.
Katz, L. N. (1941). *Electrocardiography*. Kimpton, London.
Lewis, T. (1925). *Mechanism of the Heart Beat*. London.
Singer, R., and Winterberg, H. (1922). *Wien. Arch. inn. Med.*, **3**, 329.
White, P. D. (1916). *Arch. intern. Med.*, **18**, 243.

PERSISTENT TRUNCUS ARTERIOSUS

BY

ROBERT MARSHALL

From the Royal Victoria Hospital, Belfast

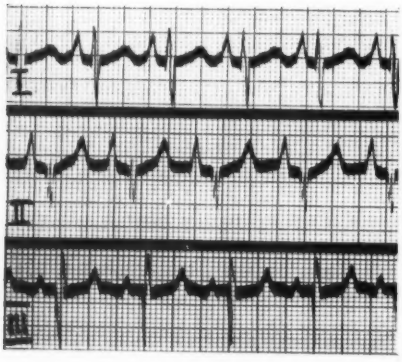
Received August 1, 1943

A boy of thirteen years was first seen at his own home on April 5, 1943. A congenital heart lesion had been diagnosed early in life: he was undersized, but showed no other congenital defect; and there was cyanosis and clubbing of fingers. He was alert, intelligent, and engaging. For three days he had been vomiting blood in small quantities, but the total loss had been considerable. When first examined his heart rate was 144 a minute, the rhythm regular, and the pulse volume very poor. The apex beat was diffusely felt in the fifth space about two and a half inches from the mid-sternum; there was no thrill; there were soft systolic and diastolic murmurs audible all over the præcordium, but these murmurs proved to be transient.

On admission to hospital the hæmatemesis ceased, his pulse rate fell to normal, and no murmur could as a rule be heard, though sometimes there was an apical systolic bruit. Congenital methæmoglobinæmia as a contributory cause for his cyanosis was excluded. His blood pressure was usually 120/70. On April 19, his red cell count was 7,500,000 and his hæmoglobin 130 per cent. His temperature was unstable with a maximum of 100° F. Hæmatemesis recurred but never in alarming amounts. On April 28, his cyanosis was more intense, and gallop rhythm was present with a heart rate of 108, but this disappeared before his death from congestive failure on May 13.

The electrocardiogram showed large P waves in leads I and II; the S waves were approximately twice the amplitude of the R waves in leads I and III with splintering of QRS in II (Fig. 1).

An X-ray picture of the chest by portable apparatus showed " an enlarged globular heart of congenital type " (Fig. 2).



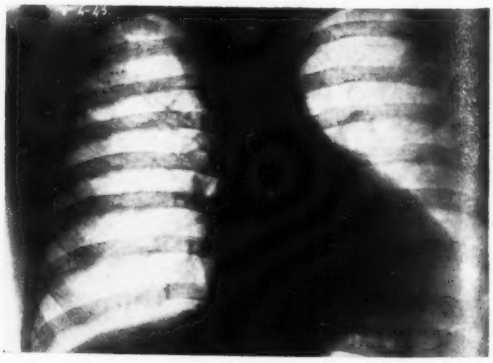


FIG. 1 and 2.—Electrocardiogram and radiogram (see text).

The transient murmurs made clinical diagnosis of the nature of his malformation difficult. The hæmatemesis was correctly attributed to œsophageal varices.

Necropsy Report

The heart was rather bulbous in shape. The longitudinal and transverse measurements being about the same—three and a half inches.

The transverse enlargement was entirely in the right ventricle, which completely covered the left ventricle when the heart was viewed from the front. The right auricle was very large and passed upwards and forwards in front of the aorta. The aorta was normal in appearance for its first one and a half inches and was only very slightly displaced to the right. There was no pulmonary artery arising from the right ventricle; instead a large arterial trunk arose from the left side of the aorta about one and a half inches from its origin (Fig. 3). This pulmonary trunk divided into a right and left artery after a course of about one and a half inches. The superior and inferior venæ cavæ emptied into the right auricle and the pulmonary veins emptied normally into the left auricle which was very small. The major branches of the aorta arose in their usual sites from the aortic arch.

The epicardium was normal and the sub-epicardial fat was considerable in amount. The veins in it were rather prominent.

On dividing the heart in its long axis through auricle and ventricle, the right auricle was found to be dilated and there was a large patent foramen ovale. The myocardium was hypertrophied, and the musculi pectinati were enormously hypertrophied. The auricular appendage between the musculi pectinati was very thin and almost transparent. The tricuspid valve was normal. The muscle of the right ventricle was hypertrophied and measured 2 cm. in thickness. The ventricular septum was slightly thicker. There was a complete absence of the membranous septum and the conus arteriosus was absent (Fig. 4). The blood must have passed through the deficient membranous septum to the aorta. The left auricle was very small and the myocardium was not hypertrophied. The mitral valve was normal and the left ventricular wall was slightly thicker than normal. The aorta opened from this

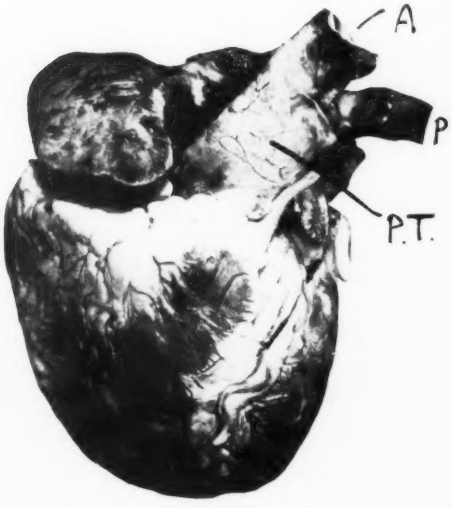


Fig. 3.—Anterior aspect of the heart showing enlarged right auricle and ventricle. P.T.=persistent truncus arteriosus. A=aorta. P=pulmonary artery.

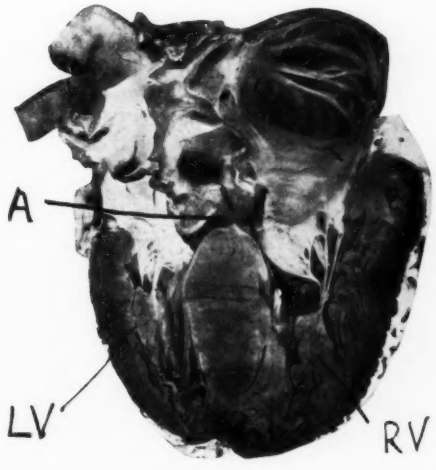


Fig. 4.—The heart on section, showing the absence of the pars membranacea of the interventricular septum.

ventricle and apparently the blood which reached it from the right ventricle did so through the deficient septum rather than because of dextroposition of the aorta. The aortic valve was tricuspid and competent; the cusps did not present a " fleshy " appearance and all the heart valves were free from endocarditis.

Comment

Of 1000 cases of congenital cardiac malformation analyzed by Maude Abbott (1932), 21 showed persistent truncus arteriosus; the oldest subject lived to twenty-five, but the average age at death was four years; hypertrophy of the right ventricle was found in 15 and of the left ventricle in 11 cases; dextroposition of the aorta was found in 19 cases. In the case now described it was at first thought that there was no dextroposition but on closer scrutiny it was considered that the truncus was slightly superimposed on the right ventricle and not altogether on the left. Brown (1939) agrees with Humphreys (1932) in describing five types:

(1) Partial common trunk with ductus arteriosus.
(2) Partial common trunk without ductus arteriosus.
(3) Complete common trunk with independent origin of pulmonary arteries.
(4) Complete common trunk with one pulmonary artery and a bronchial artery.
(5) Complete common trunk with no sixth arch derivatives and bronchial arteries.

The present case appears to be of Humphreys' fourth type, the single pulmonary artery arising as a branch from the common trunk and then dividing into right and left branches. Maude Abbott stated that four valve cusps of " fleshy " type are to be expected on embryological grounds but that tricuspid valves have been described in a number of cases including two of her own series. Brown quotes Ross (1935) that the cusps differ from normal cusps by the absence of elastic tissue and their general structure of myomatous tissue, and this finding was confirmed by Abbott. In the present case the three cusps were normal to both naked eye and microscopic examination.

Summary

A persistent truncus arteriosus was found after death in a boy aged thirteen years, who had always been cyanosed and breathless, and had suffered from hæmatemesis due to œsophageal varices. The cardiac murmurs had been transient; there was no endocarditis and death was attributed to congestive failure. Electrocardiogram, radiogram, and post-mortem findings are recorded.

I wish to thank Professor J. H. Biggart for his valued opinion, Dr. C. R. Murdock for the necropsy report, Dr. F. C. Montgomery for the radiogram and Mr. A. M. Mahaffy for photographs of the heart.

References

Abbott, M. E. (1936). *Atlas of Congenital Heart Disease*, New York, p. 60.
Brown, J. W. (1939). *Congenital Heart Disease*, London, p. 181.
Humphreys, E. M. (1932). *Archiv. Path.*, **14**, 671.

COARCTATION OF THE AORTA, DOUBLE MITRAL A-V ORIFICE, AND LEAKING CEREBRAL ANEURYSM

BY

J. N. P. DAVIES AND J. A. FISHER

From the University of Bristol

Received August 18, 1943

The purpose of this paper is to record and discuss the case of a boy with well-marked coarctation of the aorta, who made a complete recovery from subarachnoid hæmorrhage due to a leak from an intracranial aneurysm, only to die from rupture of a dissecting aortic aneurysm. A double mitral auriculo-ventricular orifice found at autopsy in this case is an extremely rare cardiac anomaly, only ten previous cases having been recorded (Abbott, 1927). In the present case the occasional diastolic or presystolic mitral murmur may have been the clinical counterpart of this anomaly. We can find only two previous cases in which recovery from a subarachnoid hæmorrhage in association with coarctation has been recorded—one in a girl, aged 12, reported by Lichtenberg and Gallagher (1933), and the other in a woman of 25, reported by Baker and Sheldon (1936)—and in neither case was the cerebrospinal fluid available for examination.

Clinical Features

The patient, R. W., was found to have abnormal heart sounds at the age of five years during a routine examination at a school clinic. He remained under observation, first of Dr. Carey Coombs and later of Professor Bruce Perry, until the age of 14, when he left school. During this period health and growth were normal and there were no relevant subjective symptoms. The cardiac lesion caused no apparent disability except that sometimes after exercise he became cyanosed. Its nature was not firmly established for some years. A loud apical systolic murmur was present constantly and it was noted that there was also from time to time another apical murmur which was mid-diastolic or presystolic in character; because of the latter murmur the possibility of a rheumatic origin was considered. From 14 to 17 years of age he worked in a factory, where his work included vigorous physical exertion, such as the moving of heavy packing cases: he had infrequent attacks of headache and vomiting. Later he worked as an A.R.P. messenger and he rendered good service during the air raids on Bristol. At the age of 17 years, on July 10, 1941 he had a sudden fainting attack, details of which are not available. On July 15, he had a severe attack of vomiting, lasting a few hours and followed, on the evening of the next day, by a sudden violent frontal headache attended by neck rigidity; this persisted until his admission to hospital on July 17, with a tentative diagnosis of acute meningitis. On examination in hospital the patient, a strongly built youth, had slow slurred speech and slow cerebration. Temperature and pulse and respiratory rates were normal. There was marked neck rigidity and Kernig's sign was positive on both sides, but there was no head retraction, and the abdominal and tendon reflexes were normal, and the plantar reflex on both sides was flexor. There were no signs of cranial nerve lesions, and the motor and sensory systems appeared normal. The cerebrospinal fluid was heavily blood-stained and under slightly increased pressure. 60 c.c. were withdrawn; three tubes were used to collect the fluid and in each the proportion of blood appeared to be about the same; it was free from clot. There was no relative increase in leucocytes; the protein was 20 mg.; chlorides, 760 mg.; and urea, 43 mg.; each per 100 c.c. On centrifugalization the supernatant fluid was quite clear and colourless.

Cardiovascular system.—The apex beat was very forcible and was situated in the fifth left interspace, one inch outside the mid-clavicular line. The first heart sound was completely replaced by a loud prolonged rasping murmur heard all over the præcordium. Pulsating vessels could be seen and felt in many areas of the chest wall, particularly, on both sides of the sternum, near the anterior axillary folds, over the upper part of the rectus sheath, and at the back between the inner borders of the scapulæ. A murmur similar to the cardiac murmur could be heard over many of the dilated super-

ficial arteries and was particularly marked just above and medial to the angle of the right scapula. The radial pulses were equal, full, and bounding, and the blood pressure in both arms was 220/120. The pulse in the femoral arteries could not be felt although a slight pulsation was felt in the left dorsalis pedis artery. The systolic blood pressure in the legs could not be determined accurately, the readings varying between 120 and 130; the diastolic pressure could not be determined. The lungs appeared normal and there were no other relevant findings.

On July 18 he was much better. The headache had gone. Slight ptosis of the left eyelid was observed. The cerebrospinal fluid was blood-stained, the pressure normal, the supernatant fluid straw-coloured, protein 25 mg., urea 43 mg., sugar 71 mg., each per 100 c.c. No relative increase of leucocytes, Wassermann reaction negative, culture sterile. A small quantity of cerebrospinal fluid was withdrawn twice daily for the next few days; the fluid became progressively clearer. On July 20 the neck rigidity had disappeared, the ptosis was diminished, and the speech somewhat improved. Radiographic examination showed an enlarged left ventricle and the characteristic notching of the ribs. No enlargement of the aortic arch could be seen. Progress continued satisfactorily and when he was discharged from hospital on August 16, 1941, he was mentally normal, his speech was normal, and there was no ptosis of the eyelid. At no time was there any elevation of temperature, pulse, or respiration. He seemed strikingly untroubled by his grave cardiac lesion and he presented the robust physique commonly associated with the so-called adult type of aortic coarctation. He returned to work and remained well, without headaches, for the next 13 months. He was, however, found dead in bed one morning, having died sometime during the night: he had felt perfectly well when going to bed on the previous evening.

Pathological Examination

The body was that of a well-nourished and well-developed youth. There were no external abnormalities. The serous cavities, with the exception of the pericardium, were normal, and the internal organs with the exceptions described below, appeared normal apart from a moderate acute congestion. The thymus weighed 45 grams.

Heart and Aorta. The main features were a supernumerary mitral valvular apparatus, a marked hypertrophy of the left ventricle, bicuspid aortic valves, fusiform dilatation of the ascending aortic arch with dissecting aneurysm and consequent rupture into the pericardial sac, almost complete coarctation of the so called adult type, and anomalous great vessels (Fig. 1).

The heart weighed 550 grams, mostly the result of a well-marked hypertrophy of the left

Fig. 1.—To show the coarctation, and the four vessels arising from the aortic arch. The arrow points to the rupture of the intima.

ventricle, the wall of which was 20 mm. thick. The left auricle appeared normal. The main mitral valve ring was 55 mm. in circumference. In the middle of its aortic cusp there was a complete accessory or supernumerary mitral apparatus, the ring of which was 45 mm. in circumference and furnished with two cusps which had a line of closure at right angles to that of the main mitral cusps. The accessory cusps were well supplied with chordæ tendineæ and papillary muscles; the cusps were well-developed, forming a narrow elongated cone (Fig. 2).

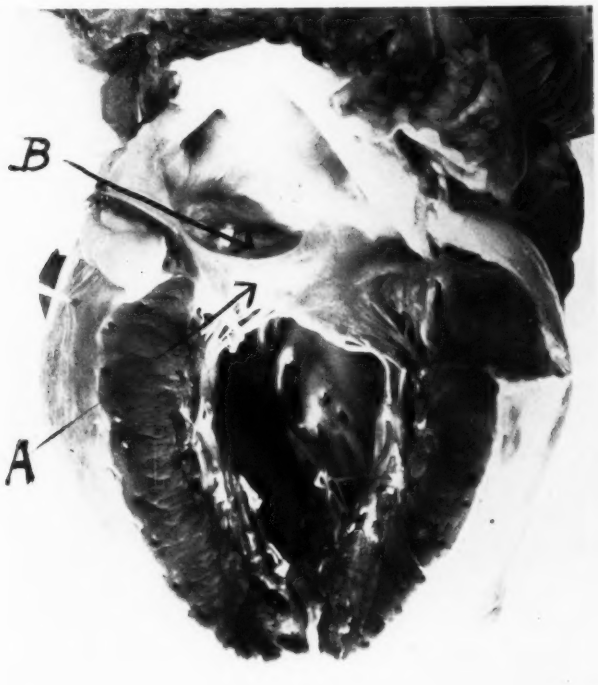


FIG. 2.—To show the double auriculo-ventricular mitral orifice, the left ventricle and the left auricle have been cut open and one cusp of the mitral valve divided and cut away. Facing is the aortic cusp of the mitral valve (marked A) with the supernumerary orifice: at the base of the opening (marked B) a small part of the left ventricular cavity can be seen.

There was no sclerosis or fenestration of any of the heart valves. The bicuspid aortic valves showed a slight diffuse thickening which rendered them more opaque than normal. The valve ring was 90 mm. in circumference. Both coronary arteries arose from the posterior cusp and there was no raphe in either aortic sinus. There were no other notable findings in the heart. The other measurements were: right ventricle, 5 mm. thick; circumference of the tricuspid ring, 100 mm., and of the pulmonary ring, 70 mm.

In the ascending aorta the fusiform dilatation showed a maximum circumference of approximately 130 mm., the aorta narrowing at the site of origin of the great vessels to a circumference of 25 mm. At the origin of the foetal isthmus there was a further considerable narrowing, the diameter showing a maximum of 5 mm.; the isthmus continued as a cone-shaped tube to the site of the coarctation, which admitted a hair-like probe after some manipulation. The site of the coarctation was at the attachment of the obliterated ductus. Below the coarctation the aorta rapidly widened to a circumference of 38 mm. The great vessels arose from the arch in four main branches which could not be traced out under the circumstances of the autopsy.

A dissecting aneurysm originated in a linear breach of the aortic intima, 35 mm. in length, and commencing 20 mm. above the posterior aortic cusp. The dissecting aneurysm extended, by a splitting of the media, from the root of the aorta to the origin of the great vessels to form a cuff-like sheath of blood. At a point in the aorta opposite the origin of the dissection the blood ruptured outwards into the pericardial cavity, resulting in a hæmopericardium, which was the immediate cause of death. Histologically (Fig. 3), at the site of origin of the dissection, there were numerous focal defects of elastic tissue in the media and the blood had ruptured

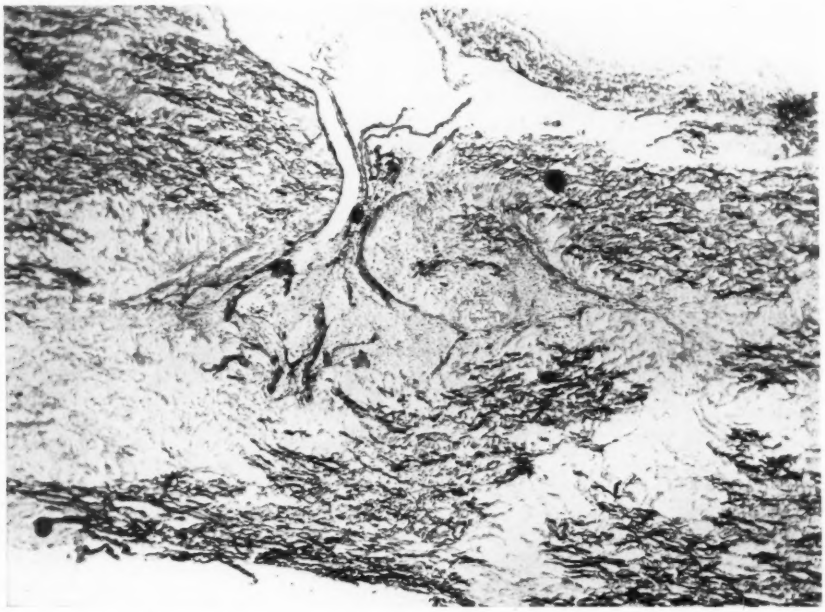


FIG. 3.—Aorta at the site of rupture through the intima, showing the beginning of the dissection. Magnification ×50.

through the intima into one of these breaches in the elastica. Similar focal defects with replacement by hyaline collagenous material were observed in sections taken from the ascending aorta in other sites and in a section from the aorta below the coarctation.

Below the coarctation the intercostal arteries showed considerable enlargement; at the orifices of these arteries there were a few smooth yellow patches of atheroma in the aortic intima. There was also an occasional yellow streak of intimal atheroma, both above and below the coarctation. There was no fatty intimal change at or near the origin of the dissecting aneurysm.

In the brain there was a berry aneurysm 1 cm. in diameter (Fig. 4), situated on the left middle cerebral artery just beyond its first main division as it passed on to the island of Reil. Above this berry aneurysm, about 4 cm. distant, there was a cyst in the brain substance which contained a faintly brown fluid. The cyst was about 2 cm. in diameter and the wall showed a deep yellow pigmentation. The adjacent pia-arachnoid showed a similar discoloration. No aneurysm could be identified in the small artery which passed into the wall of the cyst, but it appeared most likely that this lesion resulted from a leakage from a second aneurysm rather than from the aneurysm several centimetres distant. No other abnormalities were found in the brain or the meninges. Numerous sections of the arteries forming the circle of Willis were examined microscopically. Occasional defects of the muscular coat were observed of the type commonly found in normal subjects. Sections stained by Verhoeff's elastic tissue stain

FIG. 4.—Cross-section of brain to show the aneurysm and the area of hæmorrhagic infarction.

followed by a modification of Masson's trichrome stain showed several irregularities and breaches in the internal elastic lamina reminiscent of the elastica defects in the aorta (Fig. 5). There was no atheroma of the cerebral vessels.

The left kidney weighed 200 g.; the right, 207 g. In both the capsule stripped easily leaving a smooth underlying surface. On section the normal architecture was clearly defined and there was moderate acute congestion. There was a normal proportion between cortex and medulla, the ratio being approximately 3 : 1. The main renal arteries appeared normal. Apart from acute congestion, no pathological change was observed. Several sections of the kidneys stained with Masson's trichrome stain were examined with the object of observing the Goormaghtigh bodies. No hypertrophy or hyperplasia of the Goormaghtigh cells was observed, and Lieut.-Colonel F. Bayless, U.S.A.M.C., kindly examined the sections and confirmed this observation. The small arteries and arterioles showed no muscular hypertrophy or other change.

DISCUSSION

The association between intracranial aneurysm and coarctation is an interesting one. Abbott (1928) considered that an intracranial aneurysm was most probably present in all cases of coarctation terminating with an intracranial hæmorrhage before the end of the second decade, where there was no history of infection or other apparent cause. She estimated that intracranial hæmorrhage was the cause of death in about 10 per cent of cases of the so-called adult type. In view of the high cephalic blood pressure in coarctation it is not surprising that recorded clinical cases of recovery from intracranial hæmorrhage with associated aortic coarctation are so very rare. In the present case the diagnosis of subarachnoid hæmorrhage was established by the finding of blood-stained cerebrospinal fluid. This fluid was obtained twenty-four hours after the onset of violent headache and neck rigidity, which was presumably the result of blood leaking into the subarachnoid space. The fluid showed an even

admixture of blood, with no clot and without variation in three successive samples from the first puncture, and the supernatant fluid was quite clear. Merritt and Fremont-Smith (1937) state that the cerebrospinal fluid will be yellow or xanthochromic if it has contained blood for more than four hours before removal. We consider that the evidence in this case is strongly in favour of the blood not being traumatic in origin and that it suggests that exceptions can occur to Merritt and Fremont-Smith's generally accepted statement. In the case under discussion subsequent specimens showed considerable hæmolysis.

An underlying factor common to intracranial aneurysm and aortic coarctation can now be considered in view of Glynn's (1940) observations on elastic tissue defects in intracranial arteries associated with aneurysm. Glynn directs attention to the importance of lesions of the elastic elements in the intracranial arteries in the genesis of these aneurysms, pointing out that the medial muscular defects can have little ætiological significance, occurring as they do in about 80 per cent of the population. He confirms that there is a peculiar concentration of the elastic tissue into the internal elastic lamina in the muscular cerebral arteries. From inflation experiments he shows that the unsupported internal elastic lamina can withstand a pressure twice as high as the highest recorded in cases of high blood pressure, and he suggests that the main strength of these vessels, concentrated as it is into one inner layer, is very susceptible to injury such as encroachment by atheroma; and he thinks it justifiable to conclude that this topographical peculiarity is also responsible for aneurysm formation as a result of non-atheromatous degeneration of elastic fibres. In view of Glynn's work we examined several serial sections of the circle of Willis in our case and found a considerable number of areas in which the internal elastic lamina showed a focal thinning or interruption, sometimes with replacement by hyaline fibrous tissue. An example of such a defect is illustrated in Fig. 5,

FIG. 5.—Breach of internal elastic lamina. Circle of Willis artery. Staining, Verhœff, and Masson. Magnification × 155.

and until we have the opportunity of examining an adequate series of normal cases to serve as controls we are unable to indicate their precise significance; but they are sufficiently striking to merit further attention, and they direct attention to a single pathological process which may be common to two anomalies having a marked clinical association, notably intracranial berry aneurysm and coarctation of the aorta. We consider that the weakening of the internal elastic lamina, which we believe existed in our case, is a condition similar in ætiology to the focal hyaline defects in the elastic tissue in the aorta. These defects were found microscopically in 12 out of 13 cases of rupture of the aorta reviewed by Abbott (1928), and they were present in our case above and below the coarctation (Fig. 6). There is no reasonable doubt

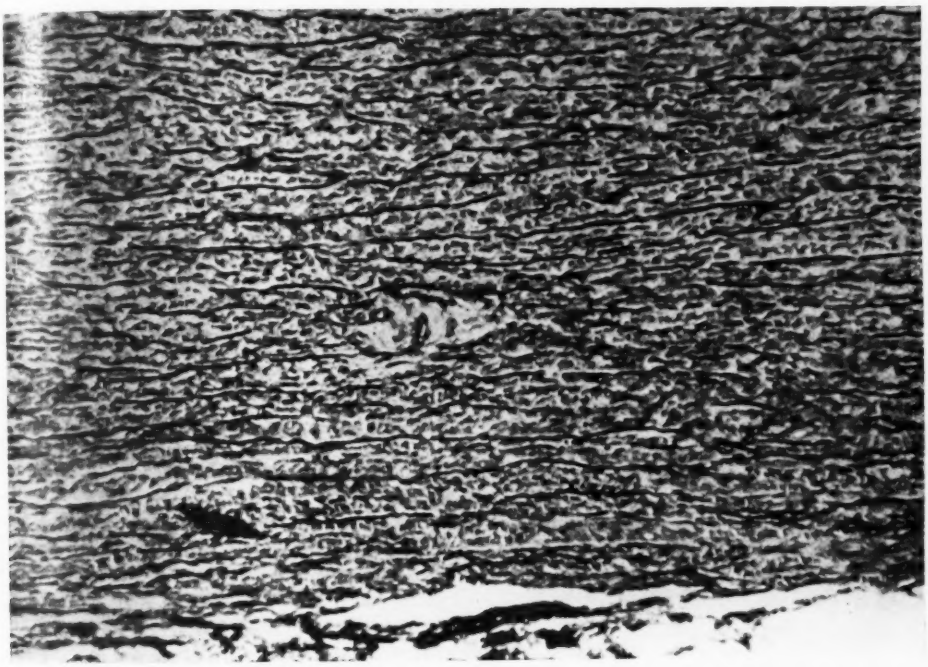


FIG. 6.—Elastica defects below the coarctation. Similar defects were shown in a micro-photograph above the coarctation, some distance from the point of rupture, but the figure has not been included. Magnification ×50.

that these defects in the aorta, congenital in origin, are the ætiological factor in the great majority of cases of aneurysm and rupture of the aorta associated with coarctation. They provide a striking parallel to the weakness of the elastica in the cerebral vessels. Shennan (1934) in reviewing 300 cases of dissecting aneurysm of the aorta decided that primary degenerative changes in the media were the most important factors and that some degree of stenosis of the aortic isthmus was not uncommon; in some of his cases there were symptoms suggesting a local lesion in the brain.

Clinically the occasional diastolic or presystolic heart murmur was possibly due to the supernumerary mitral valve. This murmur made it necessary at one period to consider the presence of rheumatic heart disease; that was, however, excluded at the autopsy. There is some obscure relationship between the aortic calibre and the presence of double mitral orifice for in two of the ten cases of double mitral orifice previously reported (Abbott, 1936) there was an associated aortic hypoplasia. The present case emphasizes this association, but we are unable to suggest any reason for its occurrence. Anatomical opinion that we have sought

considers that the two abnormalities cannot be explained satisfactorily on a single aberrant embryological process.

Summary

The case is reported of a male, aged 17, with coarctation of the aorta and other congenital defects. He developed a cerebral hæmorrhage from a berry aneurysm, and made a complete recovery from this, only to die later from rupture of the aorta.

The autopsy revealed that, in addition to the coarctation of the aorta and associated defects of elastic tissue, there was a double mitral valve. The probable counterpart during life of this rare anomaly was a presystolic or diastolic murmur in the mitral area.

The relationship of these defects is briefly discussed.

We wish to thank Professor C. Bruce Perry for his clinic notes and Mr. T. J. H. Cooke who took the photographs.

References

Abbott, M. (1927). *Osler and Macrae, Modern Medicine*, Kimpton, London, 1927.
—— (1928). *Amer. Heart J.*, **3**, 392.
—— (1936). *An Atlas of Congential Heart Disease*, American Heart Association.
Baker, T. W., and Sheldon, W. D. (1936). *Amer. J. Med. Sc.*, **191**, 625.
Glynn, L. E. (1940). *J. Path. Bact.*, **51**, 213.
Lichtenberg, H. H., and Gallagher, H. F. (1933). *Amer. J. Dis. Chil.*, **1**, 1253.
Merritt and Fremont-Smith (1937). *The Cerebrospinal Fluid*, Saunders, London, 1937.
Shennan, T. (1934). *Med. Research Council Special Report*, Series No. 193.

TRIPLE HEART RHYTHM*

BY

WILLIAM EVANS

From the Cardiac Department of The London Hospital

Received August 28, 1943

Triple heart rhythm stands for the cadence produced when three sounds recur in successive cardiac cycles, just as two sounds compose the familiar dual rhythm of cardiac auscultation, and more rarely, four sounds a quadruple rhythm.

The conflicting views on the subject have long served to discourage attempts at a clinical perception of the problem. Disagreement is perhaps best illustrated by recounting the varied terminology employed to describe it. Thus we have gallop rhythm, canter rhythm, and trot rhythm; presystolic gallop, systolic gallop, protodiastolic gallop, and mesodiastolic gallop; complete summation gallop and incomplete summation gallop; auricular gallop, ventricular gallop, and auriculo-ventricular gallop; true gallop; left-sided gallop and right-sided gallop; rapid-filling gallop; diastolic echo; mitral opening snap; reduplication of first sound and reduplication of second sound; Potain's murmur; third heart sound and fourth heart sound. Others may have escaped my notice. This muddled nomenclature, as long as it stands, will frustrate any attempt to unify the many views held on triple rhythm. There is need of a simplified terminology based on clinical findings. It is indeed clear that a neglect of the clinical aspect on the one hand, and a persistence on the part of many to explain the *mechanism* of the supernumerary sound on the other hand, and to classify triple rhythm in accordance with sound records, have been largely responsible for obscuring this common form of cardiac rhythm. Phonocardiography need not become a routine test in clinical cardiology; when it has helped to establish a classification of triple rhythm it will have achieved its main purpose, though it will still serve in other auscultatory problems. In the present investigation it has been a condition that the supernumerary heart sound should be elicited first by clinical auscultation. No phonocardiogram was taken as a preliminary test, and it was only recorded later in order to confirm or correct the clinical impression that had already been gained.

Among patients attending the Cardiac Department of the London Hospital during a recent period, and known to have heart disease or referred for an opinion on the heart, there were 270 who presented triple rhythm. These were placed in a special series for which a set method of inquiry had been prepared. A regularized history was taken and a general examination was made. A special record was taken of the heart rate at rest and after exercise, the presence of cardiac enlargement, the symptoms and signs of heart failure, and the blood pressure. As to the supernumerary sound, its site, distribution, and character, were separately noted, as well as the effects upon it of respiration, change of posture, and induced tachycardia. The apical impulse was examined by palpation and direct auscultation. Cardioscopy was a routine method of examination by which the size of the separate heart chambers was assessed. At the start certain measurements were taken; these included the width of the heart and thorax, and the height of the right auricle and diaphragm, but they were discontinued when it was realized that they brought no valuable information. Sometimes, however, use was made of

* The third Strickland Goodall Memorial Lecture delivered before the Worshipful Society of Apothecaries in London, June 24, 1942.

the distance between the junction of the right auricle and superior vena cava and the summit of the pulmonary arc, for it partly expressed the degree of pulmonary artery distension when present. In certain patients a limb lead electrocardiogram was always taken. A phonocardiogram by a Cambridge string galvanometer and the electrocardiogram were taken simultaneously on the same plate.

In addition to the series of patients with triple rhythm, 200 subjects were added in due course to serve as control cases for this investigation of certain types of triple rhythm.

Classification

I do not intend to deal here with a complete bibliography of the subject because a faithful account of it was recorded by Holt (1927). Of course I shall refer to the work of many of those who before and since have described their clinical and graphic findings in patients with triple rhythm, and have thus contributed much to our knowledge of the problem. Particularly do I want to mention the astute observations of Potain (1856, 1866, 1876, 1880, 1894, and 1900) in pre-phonocardiographic days more than half a century ago. He differentiated between gallop and split sounds. A reduplicated or split sound, he said, was one where the two components had the same quality and pitch and were separated one from the other by a very short interval, while a gallop rhythm had a sound added to the normal sounds, and separated from them by an appreciable interval. The added sound was usually short and dull, a sort of thud, often better felt than heard, and frequently missed if auscultation was carried out with a stethoscope alone, monaural though it was. Usually it was detected in the region between the apex, the left border of the sternum, and the second rib, and it was sometimes heard over a limited area. The added sound was always diastolic and according to its position it could be described as protodiastolic, mesodiastolic, or presystolic. The typical gallop was presystolic; the protodiastolic gallop presented a diastolic echo and could be likened to the recall on the drum or a rebound of a hammer on the anvil.

The term gallop rhythm has become rooted in the history of triple heart sounds and most writers have adopted it. But since the qualifying terms gallop and canter only imply that the rhythm initiated by three sounds in the cardiac cycle is simulated by the sounds produced by a moving horse, and since adherence to such terms prevents a modern understanding of this form of cardiac rhythm, I mean to discard them. Instead it is only necessary to appreciate that when a supernumerary sound in the cardiac cycle gives rise to triple rhythm, three types may be recognized according to the position of the adventitious sound.

In the *first type* the added sound is found early in cardiac diastole; it follows the second sound immediately and is the third sound in the cardiac cycle. In the *second type* the added sound occurs late in ventricular diastole; it succeeds the period which the third sound customarily occupies, immediately precedes the first heart sound, and therefore may be styled the fourth sound. Thus the third sound disturbs the early part of the silent diastolic period, and the fourth sound disturbs the end part. In the *third type* the added sound is situated towards the end of systole just before the second heart sound. The position of the adventitious sound in the respective types is usually determined readily by auscultation even in the presence of moderate tachycardia. Severe tachycardia may be a distinct handicap although even then a classification of triple rhythm can usually be determined, and especially when aided by ancillary clinical data, but short of phonocardiography. A scheme setting out the positions occupied by these supernumerary sounds in the cardiac cycle is shown in Fig. 1.

The clinical conditions which give rise to the supernumerary sounds have been arranged according to the type of triple rhythm which they constitute, and this arrangement suggests a classification of triple rhythm.

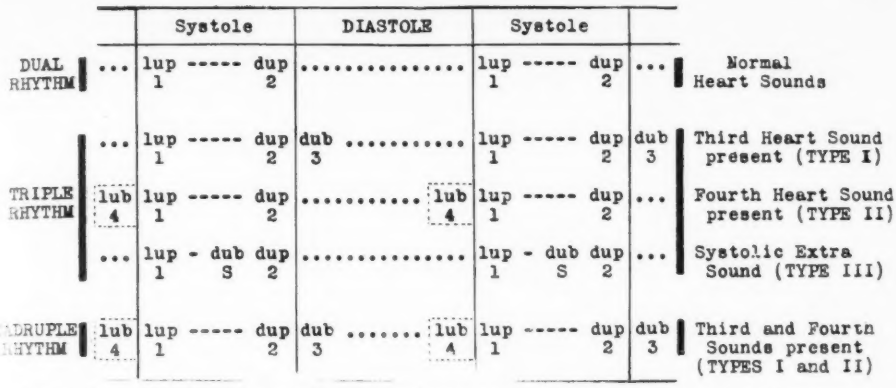


FIG. 1.—Scheme showing position of heart sounds in cardiac cycle in different types of triple rhythm. S—systolic extra sound. Fourth heart sound occurs in *ventricular* diastole, but in *auricular* systole.

TABLE I

THE CLASSIFICATION OF TRIPLE HEART RHYTHM

		No. of cases
Type I.—Addition of the third heart sound		205
(*a*) In health	125	
(*b*) In right ventricular failure	80	
Mitral stenosis	44	
Hypertension	16	
Thyroid toxæmia	8	
Congenital heart disease	7	
Emphysema	5	
Type II.—Addition of the fourth heart sound		60
(*a*) In delayed A-V conduction	14	
(*b*) In left ventricular failure	46	
Hypertension	41	
Aortic incompetence	5	
Type III.—An extra heart sound in late systole		5
	Total 270 cases	

The special clinical and graphic features of the three types of triple rhythm will now be described.

TYPE I.—ADDITION OF THE THIRD HEART SOUND

When the third heart sound becomes audible in successive cardiac cycles, a form of triple rhythm designated here Type I, is established. As long ago as 1855 Stokes reported a case in which an early diastolic sound was heard, but it was A. G. Gibson (1907) and Hirschfelder (1907) who independently discovered that a wave in the venous tracing was associated with a sound in early diastole. Gibson found that this " b " wave, placed between the " v " and " a " waves, was seen at its best in healthy young adults, and in two of these he detected a sound between the second and the succeeding first sound. He said that it was not easy to hear, but was most distinct in the short interval between expiration and inspiration, and when pressure was applied to the abdomen. Gibson informed Einthoven of his discovery and the latter (1907) recorded a sound which corresponded in position with Gibson's " b " wave and Hirschfelder's " h " wave.

I have assembled 205 cases that on clinical examination showed triple rhythm due to the appearance of the third heart sound. Of these 125 were healthy subjects, while the remaining 80 had some form of heart disease.

Before defining the precise position of the third sound in the cardiac cycle it is necessary to describe the normal phonocardiogram of dual rhythm and the relation of the separate phases of the tracing to the electrocardiogram. Thus, the auricular sound in health starts, as a rule, at the end of the P wave and merges into the ventricular part of the first sound which

starts near the S wave and never in front of the R wave. The second sound begins at the end of the T wave (Fig. 2).

Type Ia.—The Third Heart Sound in Health

Einthoven (1907) found that the third heart sound in healthy subjects commenced 0·10 to 0·15 sec. after the onset of the second sound, and Lewis (1912) confirmed this. The average in my series was 0·19 sec. (Fig. 3). I have found no value in the measurements which express

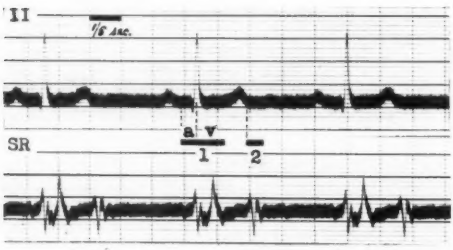


Fig. 2.—Dual rhythm. Healthy man, aged 25. In this and subsequent figures, SR is sound record, and a and v are auricular and ventricular parts of first heart sound respectively.

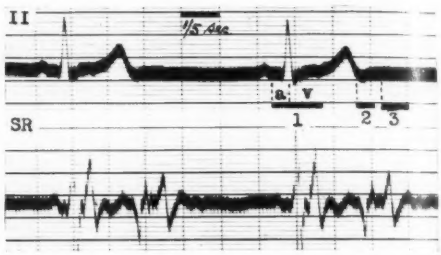


Fig. 3.—Triple rhythm, Type Ia. From a healthy man, aged 21.

the duration of the supernumerary heart sounds, but the measure of the interval between them has great value. Thus it is not unusual for this interval to become annulled and cause the third and fourth sounds to fuse from shortening of the diastolic phase by tachycardia and/or lengthening of the auriculo-ventricular period.

Mechanism. As it is of no consequence here to know the actual mechanism producing the third heart sound, little time will be spent in debating the many theories advanced to explain it, for our closest attention needs to be directed to the clinical data presented by subjects with this form of triple rhythm. It is sufficient, therefore, to recount the common views. Gibson (1907) thought that sudden distension of the ventricle by blood from the auricle accounted for the sound, implying vibration of a taut ventricular wall. Einthoven (1907) believed that it was caused by vibration of the semilunar valves. According to Thayer (1908) and Sewall (1909) the sound is produced by vibration of the auriculo-ventricular valves after they have been floated into a position of closure by blood distending the ventricles. Thus, it is not known for certain which part of the heart vibrates, but this is immaterial for a clear understanding of the more noteworthy clinical aspects.

Incidence. The incidence of this type of triple rhythm is commonly regarded as uncertain, for while many writers speak of it as a common clinical finding, others have said it is rare and some have disputed its existence. Obrastzow (1905) heard it in 90 per cent of healthy subjects, Thayer (1909) in 65 per cent of healthy young adults, Gubergritz (1925) in 93 per cent, and Steinberg (1925) in 95 per cent of healthy children. Bridgman (1915) heard the sound in 13 out of 15 healthy boys, aged 12 to 15 years, and recorded it phonocardiographically in all of them. The third heart sound was recorded in 60 out of 100 medical students in whom sound tracings were taken by Braun-Menendez and Orias (1934).

When 50 control cases with dual rhythm were collected alongside 50 subjects showing a third sound, triple rhythm was commoner than dual rhythm in subjects of 15 to 18 years of age, and only a little less common between the ages of 18 and 20. A general acceptance of the fact that this form of triple rhythm is so common in young subjects is overdue. This realization will come to us as soon as we regularize auscultation to include self-catechism having as one of its questions: " Do I hear more than two heart sounds?" Reference to the incidence of this type of triple rhythm in older subjects is scarce. Since this has an importa

bearing on differential diagnosis from other forms of triple rhythm, I sought it at all ages. Its rare appearance in older subjects became apparent. In a series of 125 where this form of triple rhythm was heard, which excluded children under 9, 115 were under 25 years. The actual incidence among the older group was as follows: 1 aged 25, 1 aged 26, 1 aged 27, 1 aged 28, 2 aged 30, 1 aged 34, 1 aged 35, 1 aged 38, and 1 aged 39. Thus triple rhythm, Type Ia, was never heard in subjects of 40 or over; it was rare over 30 (4 out of 125) and uncommon at 25 or over (10 out of 125).

Site. The third heart sound was best heard in the fourth intercostal space at a point half-way between the nipple line and the lateral border of the sternum and, therefore, a little way internal to the mitral area (Fig. 4). In two patients in whom the sound was more distinct

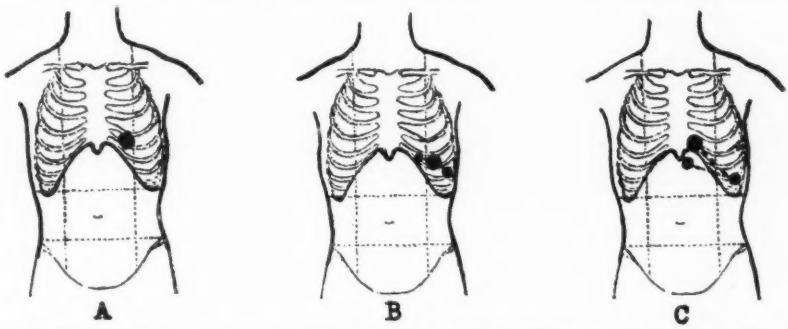


FIG. 4.—Localization of supernumerary sounds in triple rhythm. Dots and discontinuous lines indicate places of maximum intensity and distribution. (A) Type Ia, Type IIa, and Type III. (B) Type Ib. (C) Type IIb.

just outside the mitral area, the heart was found to be displaced outwards by scoliosis. The location of the sound is important because it may by itself decide the diagnosis of triple rhythm Type Ia (third heart sound in health) from Type Ib (third heart sound in disease), for in the physiological variety it is most distinct inside, and in the pathological type usually outside, the mitral area. In part, perhaps wholly, this variation in the site of maximum intensity of the sound in the two groups depends on the size of the heart, so that in the pathological states which may show a third heart sound, the apex beat is moved outwards from cardiac enlargement.

Conditions influencing the intensity of the sound. In order to bring out the third heart sound or to increase its intensity, Thayer (1909) adopted certain manœuvres which moved the apex nearer to the chest wall and accelerated the venous return to the heart. Thus he listened with the subject in the reclining posture after exercise, or inclined on his left side, or while an assistant elevated the arms and legs; he also applied abdominal pressure. I have tested all these means and found that only two consistently accentuated the third heart sound, namely the induction of moderate tachycardia, and the adoption of the reclining posture. In all 125 subjects with triple rhythm, Type Ia, the sound was best heard in the reclining posture, and in 90 the sound actually disappeared as the subject assumed the upright position. In 22 of the 35 cases in which the sound persisted in the upright posture, its audibility only lasted as long as the tachycardia induced by the change of posture lasted.

The influence of posture on this triple rhythm also helps materially to decide which variety is present, whether Type Ia or Type Ib. This in Type Ib the third sound is heard in both upright and reclining postures, whereas in Type Ia the sound usually disappears in the upright posture unless tachycardia is present (Fig. 5). Presumably this characteristic influence of posture is related to pressure within the right heart so that in the pathological type of triple rhythm the increased pressure does not fall below the threshold at which the third sound appears, even when the upright posture is adopted.

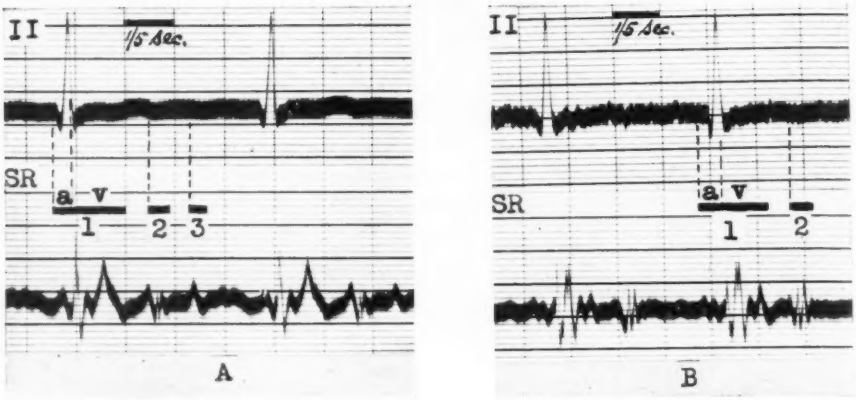


FIG. 5.—Triple rhythm, Type Ia. The third heart sound recorded in the reclining posture (A) disappeared in the erect posture (B). From a healthy girl, aged 15.

The Heart in Triple Rhythm, Type Ia

From routine cardioscopy in healthy subjects with a third heart sound, I found that the heart showed a characteristic outline. My early impression was that its most distinctive feature was enlargement of the pulmonary artery seen as a prominent pulmonary arc. Thinking that this might be part of a more general distension of the right heart I sought other signs, so that the height of the venous column in the neck was measured, and at cardioscopy a record was made of the size of the right auricle and ventricle, and prominence of the superior vena cava and hilar shadows; the height of the diaphragm and of the right auricle was measured as well as the width of the heart and thorax. Although these changes were not found consistently, yet some characteristic of the average radiological appearance of the heart in young subjects was very often preserved. Thus, there might be a squat-like appearance of the cardiac shadow, high diaphragm and shallow thoracic cage, prominence of the right auricle and sometimes of the superior vena cava, prominence of the pulmonary artery which filled the pulmonary bay, and increased density of the hilar shadows (Fig. 6). As enlargement

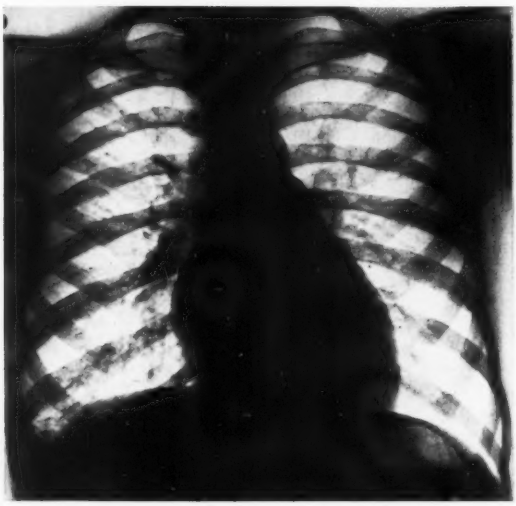


FIG. 6.—Characteristic heart outline in healthy child, aged 12. Pulmonary artery index (hereafter designated P.A. index), 6·0. This and subsequent X-rays are teleradiograms.

of the pulmonary arc was the most constant feature of the cardiac silhouette, a search was made for a means of recording the impression of the size of the pulmonary artery obtained by cardioscopy. For this purpose the distance was measured between the junction of superior vena cava and right auricle, and the summit of the pulmonary arc. This distance, measured in centimetres, is a rough estimate of the degree of pulmonary artery distension and I have named it the *pulmonary artery* (*P.A.*) *index* (Fig. 7). This value, representing as it does the width of the vascular pedicle at its base, is not an actual measure of the pulmonary artery, and two facts lessen its usefulness; the distance is increased by elevation of the diaphragm and diminished when the diaphragm is low, and the measurement is increased to the right when the ascending aorta is displaced from unfolding of its arch. Yet I have found the measurement useful as a means of recording the visual impression of the size of the pulmonary artery, although the numerical value does not always tally precisely with the judgement formed on cardioscopy which must remain as the most dependable guide in this matter.

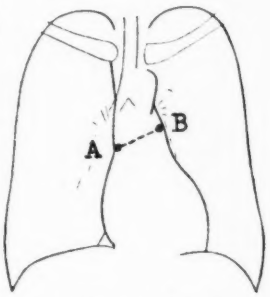


FIG. 7.—Measure of pulmonary artery distension. A, junction of superior vena cava and right auricle. B, summit of pulmonary arc. Distance AB in centimetres is *pulmonary artery* (*P.A.*) *index*.

In 50 consecutive cases over the age of 15 the size of the pulmonary artery was estimated in terms of the pulmonary artery index as well as by visual impression, and was compared with the same findings in 50 subjects of corresponding age presenting dual rhythm. In the triple rhythm series the artery was prominent in 47 as against 8 in the control group with dual rhythm (Fig. 8). In 2 cases showing prominence of the pulmonary artery (moderate in one, and conspicuous in another) in which the third heart sound was not heard by clinical auscultation, the phonocardiograph recorded the sound. Although some degree of pulmonary artery enlargement was found in a few cases (8 out of 50) in which no third heart sound was heard,

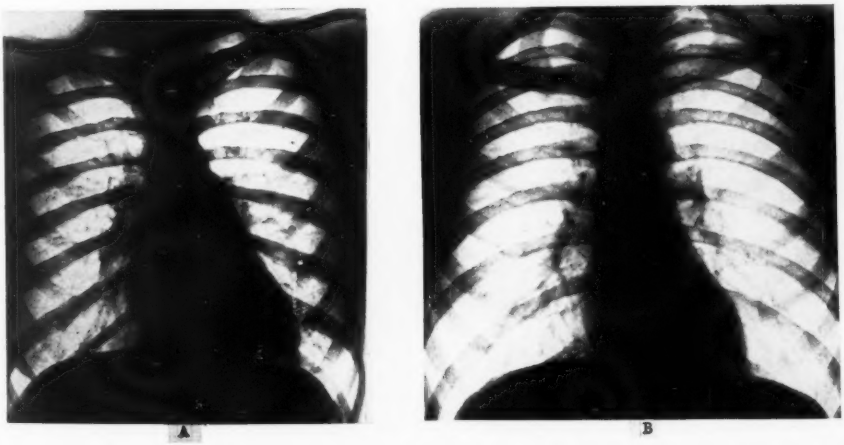


FIG. 8.—Triple rhythm, Type Ia. Teleradiograms in two healthy subjects, aged 23. (A) with a P.A. index of 6·8 showed triple rhythm and (B) with a P.A. index of 6·1, dual rhythm. Other similar contrasted pairs were submitted but had to be omitted from consideration of space.

and no enlargement in 3 of the 50 cases in which the third heart sound was present, the incidence of this radiological finding was so common in the triple rhythm group compared with the control group with dual rhythm, that the association between pulmonary artery enlargement and triple rhythm, Type Ia, is strongly supported. I have been at some pains to

control the observation, and it is significant that 40 out of 50 cases with triple rhythm showed a pulmonary artery index of 6·5 or over, whereas the index was less than 6·5 in 41 out of 50 cases of the same age that showed dual rhythm (Tables II and III). The limb lead electrocardiogram in subjects in this group was in no way distinctive, but changes in the chest leads are being further examined.

TABLE II

THE SIZE OF THE PULMONARY ARTERY IN 100 HEALTHY SUBJECTS HALF WITH TRIPLE RHYTHM (TYPE Ia) AND HALF WITH DUAL RHYTHM

Age	Estimate of pulmonary artery distension at cardioscopy		Pulmonary artery index	
	Subjects with triple rhythm	Control cases	Subjects with triple rhythm	Control cases
16	+ + *	— *	7·0	5·5
16	+ +	—	7·0	5·9
16	+ + +	—	7·0	5·5
17	+	—	6·5	5·0
17	+	—	7·0	6·0
17	+ +	—	6·5	5·7
17	+	—	7·0	5·2
17	+	—	6·0	5·0
18	+ +	—	7·0	6·0
18	+	—	6·5	6·5
18	+ +	—	7·0	6·4
18	+	—	6·5	6·0
18	+	—	6·4	6·4
18	+	—	7·0	5·9
18	+ +	—	6·5	5·0
18	+ +	—	7·0	5·6
18	+	—	7·0	5·7
18	+	—	6·5	5·5
18	—	—	5·5	6·2
18	+ + +	—	8·0	6·4
18	+	—	6·5	5·4
18	+	+	6·0	6·1
18	+ +	—	6·8	5·3
18	+ +	+	7·2	5·5
18	—	—	6·2	5·5
19	+ +	—	7·0	5·8
19	+	+	6·0	6·5
19	+ +	—	7·0	5·5
19	+ +	—	7·0	4·5
19	+	—	6·5	6·2
19	+ +	—	7·0	5·2
20	+ +	—	7·6	6·5
20	+ +	—	8·0	4·5
20	+	—	7·0	6·0
20	—	—	6·0	5·5
21	+	+ + +	6·7	7·4
21	+	—	7·2	6·3
21	+	—	6·6	5·4
21	+	—	6·0	6·0
21	+	+	6·0	6·5
22	+	—	6·7	4·5
22	+	—	6·8	6·5
22	+	+	6·8	5·5
23	+ +	—	6·8	5·9
23	+ + +	+ +	7·0	7·0
24	+ +	—	7·4	6·2
24	+	—	5·8	5·5
25	+ +	—	6·8	6·0
27	+ +	+	6·8	5·8
30	+ +	—	6·7	5·2

* + + +, indicate, great distension; + +, moderate distension; +, slight distension; —, no distension.

TABLE III

COMPARING THE SIZE OF THE PULMONARY ARTERY IN 50 SUBJECTS WITH TRIPLE RHYTHM (TYPE Ia) AND IN 50 SUBJECTS WITH DUAL RHYTHM

Measure of pulmonary artery enlargement		Cases with triple rhythm	Control cases with dual rhythm
Estimate at cardioscopy	Great	3	1
	Moderate	22	1
	Slight	22	6
	No enlargement	3	42
Pulmonary artery index	Average	6·7	5·7
	Less than 5·0	0	3
	5·0 to 5·9	2	26
	6·0 to 6·4	8	14
	6·5 to 6·9	18	5
	7·0 or over	22	2

Type Ib.—The Third Heart Sound in Right Ventricular Failure

Potain (1900) considered that protodiastolic gallop was not a state where the third heart sound was accentuated, but that it was actually a presystolic gallop in the presence of tachycardia. Although admitting the similarity between the physiological third heart sound and the protodiastolic sound, Gubergritz (1925) believed that there was a difference in the quality and intensity of the sounds. Wolferth and Margolies (1933) observed no essential difference in quality, location, time relation, or influence of posture and various manœuvres on the sounds. They considered that apart from the fact that the physiological third heart sound became increasingly rare with advancing age, the only criterion available for differentiation was the state of the cardiac function; when this was abnormal the sound could be arbitrarily classed as a gallop sound, but if no abnormality was detected the sound could be regarded as a physiological third sound. Lian (1934) believed that the protodiastolic gallop was produced by an accentuation of the physiological phenomenon connected with the third heart sound. I found that this form of triple rhythm can be distinguished from the physiological type by regarding its position of maximum audibility, the effect upon it of posture, its age incidence, and the state of the heart. Thus, it was best heard in the mitral area or beyond according to the degree of cardiac enlargement (Fig. 4); although better heard in the reclining posture it was usually audible in the upright posture; it was found even in elderly patients; it was associated with disease which produces enlargement and failure of the right side of the heart, namely mitral stenosis, hypertension, thyroid toxæmia, congenital heart disease, emphysema, pulmonary embolism, and pulmonary hypertension. Not all cases with these clinical conditions have triple rhythm, and the circumstances deciding its presence will be mentioned as each condition is discussed.

As in triple rhythm of Type Ia, so in Type Ib, the limb lead electrocardiogram was not in any way distinctive, except that it sometimes showed auricular fibrillation or right axis deviation.

The Third Heart Sound in Mitral Stenosis

In no other section of triple rhythm is opinion more confused than in the one dealing with the supernumerary heart sound in mitral stenosis. Lewis (1915 and 1934) stated that a wide duplication of the second sound initiating a sort of gallop rhythm occurred especially in cases of mitral stenosis with a slow heart rate. The extra sound in the early part of a long diastole was unrelated to auricular systole because it persisted when the auricles fibrillated; it was probably due to an unusual intensification of the normal third heart sound and tended to be confined to the region of the apical impulse. Conner (1927) described 10 patients, 4 with severe mitral stenosis, in whom he found an unusual variety of gallop rhythm; the supernumerary sound in early diastole was so exaggerated as to dominate the auscultatory findings resulting in a sound much louder than the two heart sounds which preceded it. White (1931) said that the protodiastolic gallop produced by accentuation of the third sound of the heart was relatively rare in mitral stenosis since it was masked by the diastolic murmur. Wolferth and Margolies (1933) differentiated between the opening snap of mitral stenosis and the physiological third heart sound or protodiastolic gallop, in that the snap was short and sharp, closer to the second sound, heard only in mitral stenosis, and in the third and fourth interspace over the body of the heart and not at the apex. Bramwell (1935) and Braun-Menendez (1938) regarded the gallop rhythm in mitral stenosis as the result of an exaggerated third heart sound.

Triple rhythm was specially sought in 70 patients with mitral stenosis, 25 of whom also had auricular fibrillation, and it was found in 44 (63 per cent). The added sound was heard in 21 of the 25 cases with fibrillation, and in 23 of the 45 with sinus rhythm. Thus triple rhythm was a much commoner finding with fibrillation present. Usually it was heard best towards the anterior axillary line over the displaced apex beat, but sometimes equally well in

the mitral area. The triple rhythm of mitral stenosis was always heard in the erect as well as in the reclining position. Although moderate tachycardia was found to accentuate most forms of triple rhythm, it had a deterrent effect on that of mitral stenosis with auricular fibrillation. In 14 of the 44 cases with triple rhythm the third sound was short and clear like the second sound, although generally less loud. The distance between the second and third sounds was compared with the same measurement obtained in cases of triple rhythm in health, i.e. Type Ia; in the healthy group the distance varied between 0·16 and 0·23 with an average of 0·19 sec. while in the presence of heart disease (Type Ib) it varied from 0·13 to 0·20 with an average of 0·18 sec., so the position of the third sound was the same in both the healthy and pathological groups (Fig. 9 and 10). In the remaining 30 cases the third sound was

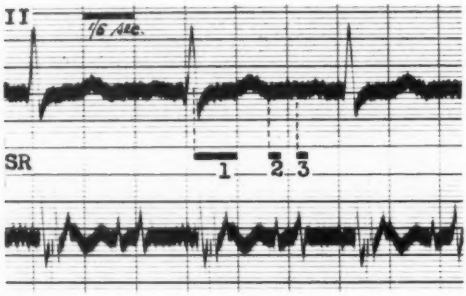


FIG. 9.—Triple rhythm, Type Ib, in a woman aged 28 with mitral stenosis. Diastolic murmur preceded first sound, and mid-diastolic murmur started at site of third heart sound.

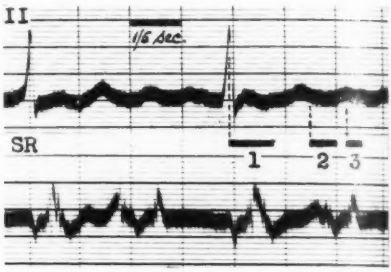


FIG. 10.—Triple rhythm, Type Ib, in a woman aged 46 with mitral stenosis and auricular fibrillation. Third heart sound was clear and not associated with murmur.

associated with the characteristic rumbling diastolic murmur of varying duration. This study of the relationship between the third sound and the mid-diastolic murmur in mitral stenosis has shown that they always coincide. I never found the diastolic murmur of mitral stenosis situated in the cardiac cycle in front of the third heart sound. It follows then that a diastolic murmur in mitral stenosis may occupy the late- or mid-diastolic period, but never the early part, so that an early diastolic murmur in the mitral area immediately following the second sound is evidence of aortic incompetence. Although the audibility of the supernumerary sound in mitral stenosis was sometimes disturbed in the mitral area by the diastolic murmur of aortic incompetence, it was never wholly obscured by it especially if auscultation was carried out towards the axilla.

An estimate of the size of the heart was made at cardioscopy in all cases of mitral stenosis that were specially examined for triple rhythm. The size of individual cavities was assessed and the presence and extent of pulmonary congestion. The pulmonary artery index was also recorded, and the results are given in Table IV. These appear to establish that in patients with mitral stenosis the finding of a triple rhythm gives some indication of the degree of cardiac enlargement. The size of the heart as a rule was least in those patients without (Fig. 11), and greatest in those with, triple rhythm (Fig. 12). When the heart was very large

TABLE IV

PULMONARY ARTERY INDEX IN 70 PATIENTS WITH MITRAL STENOSIS

Pulmonary artery index	44 patients with triple rhythm (Type Ib)	26 patients with dual rhythm
Average	8·4	6·3
Less than 7·0	5 patients	16 patients
7·0 to 7·5	10 ,,	8 ,,
7·6 to 8·9	14 ,,	2 ,,
9·0 or over	15 ,,	0 ,,

the supernumerary sound was commonly associated with the characteristic rumbling diastolic murmur. In view of this association between triple rhythm and the size of the heart it follows that this auscultatory sign does not always aid in the recognition of *early* mitral stenosis, but

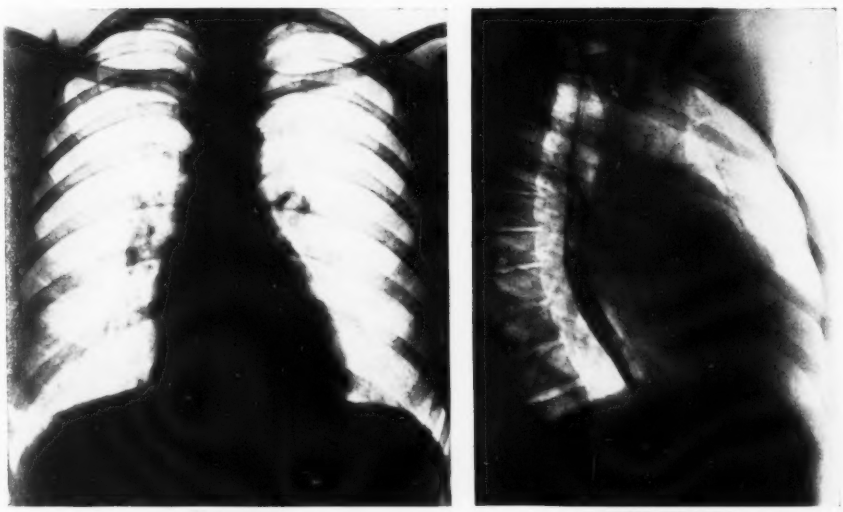


FIG. 11.—Dual rhythm in a woman, aged 24, with mitral stenosis. Teleradiogram shows slight cardiac enlargement and P.A. index of 7·6.

it can tell something of the size of the right heart and it may often provide a valuable clue in differential diagnosis. Thus, in a case with auricular fibrillation where auscultation in the mitral area finds only a systolic murmur and no certain evidence of mitral disease, the presence of this type of triple rhythm will help to establish the diagnosis of mitral stenosis. This

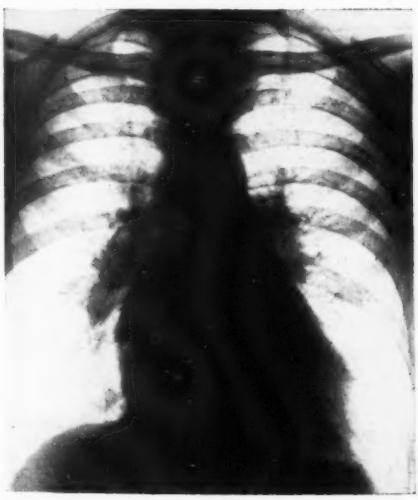


FIG. 12. Triple rhythm, Type Ib, in a man, aged 52, with mitral stenosis. Teleradiogram shows considerable cardiac enlargement and high P.A. index of 9·4.

FIG. 13.—Triple rhythm, Type Ib, in a woman, aged 18, with thyroid toxæmia. Teleradiogram shows cardiac enlargement and high P.A. index value of 8·0.

triple rhythm is also expected in the fibrillation of thyroid toxæmia, and is not uncommon in prolonged hypertensive failure with fibrillation, but I have never met it in *senile* or *mitral* fibrillation, where the heart was of normal size or thereabouts.

The Third Heart Sound in Hypertension

When heart failure makes its appearance in hypertension, triple rhythm is commonplace, but it is usually due to the presence of the fourth heart sound and not the third. Such patients are subject to paroxysmal nocturnal breathlessness and show pulmonary congestion on radiological examination. The familiar signs of right heart failure, namely, cyanosis, distension of veins in the neck, enlargement of the liver, ascites, and œdema of the ankles, are missing. When, however, left ventricular failure has been present for some time these signs often appear, and triple rhythm due to the third heart sound may then be elicited especially if tachycardia has not shortened diastole to such an extent as to cause fusion of the third and fourth sounds. This latter event has been described in a valuable paper by Wolferth and Margolies (1933) as summation gallop. Although the term is a useful one, it has limited clinical value by itself, depending as it does on findings in the phonocardiogram, and it is necessary to decide which supernumerary sound preponderates in the sound record after tachycardia has subsided. Many patients presenting triple rhythm, Type IIb, show this fusion of the two sounds; but when the effects of failure have been reduced by rest and the use of mercurial diuretics, and tachycardia has subsided with lengthening of the diastolic period

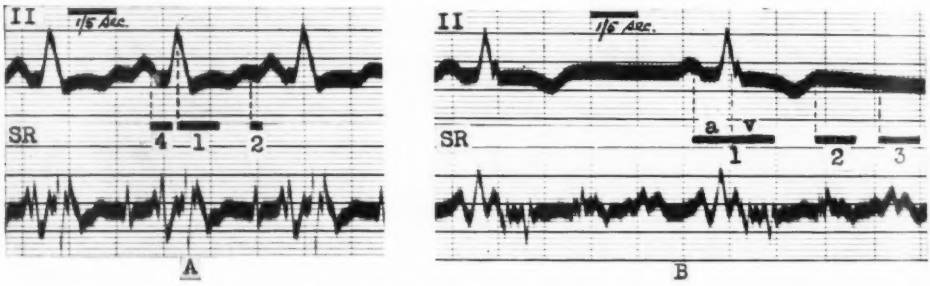


FIG. 14.—Triple rhythm, Type IIb (shown in A), changed to Type Ib (shown in B), after treatment with rest and mercurial diuretics. Male, aged 40, with hypertensive heart failure.

causing separation of the third and fourth heart sounds, the triple rhythm often changes from Type IIb to Type Ib (Fig. 14).

So far, I have found triple rhythm due to the third heart sound in 16 patients, but this does not mean that it is uncommon. Indeed, if we continue to search for this auscultatory sign in patients with hypertensive heart failure during the later phase of their illness, we shall often find it. The sound was heard best over the displaced apex beat near the anterior axilla, and although more distinct in the reclining posture it was also audible in the upright position. On cardioscopy these patients showed enlargement of the right auricle and ventricle, as well as the distension of the left ventricle and hilar congestion that constitute the earlier changes in hypertensive heart failure (Fig. 15).

Indicating, as I believe it does in hypertension, failure of the right heart as well as the left, this form of triple rhythm (Fig. 16) is a valuable sign. Of the fourth heart sound in hypertension it has been said that it is the cry of the heart for help (Obrastzow, 1905): if this metaphor is acceptable then we should recognize in the third heart sound in hypertension a more desperate appeal for assistance.

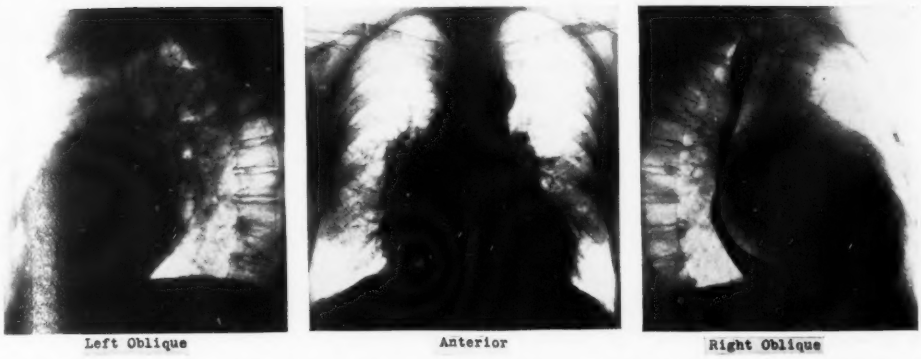


FIG. 15.—Triple rhythm, Type Ib, in a man aged 60, with hypertensive heart failure. Teleradiogram in anterior and oblique views show enlargement of right heart in addition to left ventricle, providing evidence of biventricular failure.

The Third Heart Sound in Thyroid Toxæmia

Triple rhythm due to the presence of the third heart sound was audible in the mitral area in the reclining and erect posture in 8 patients with toxic goitre. In all, tachycardia was moderate and was not regarded as a contributory factor. Hypertension was present in 2 of them. On cardioscopy some degree of cardiac enlargement and prominence of the pulmonary artery was present in 7: in 1 case there was enlargement of the left ventricle. As a rule then, when this form of triple rhythm was found in thyroid toxæmia, the heart on cardioscopy showed changes described by Parkinson and Cookson (1931). The special form characteristic of the goitre heart is based upon a combination of prominence of the pulmonary arc, the right heart, and the left ventricle. These changes are shown in a radiogram from a patient in this series exhibiting this type of triple rhythm (Fig. 13). No cardiac enlargement was found in a control series of cases with thyroid toxæmia who showed dual rhythm.

The Third Heart Sound in Congenital Heart Disease

I have never met with this form of triple rhythm in patients with congenital heart disease in the absence of right-sided cardiac enlargement. On the other hand, it has been absent in some cases showing considerable enlargement. The relationship between the actual congenital lesion, the size of the separate cavities of the heart, and the presence or absence of triple rhythm is being studied. In the meantime it may be said that triple rhythm, Type Ib, is only found in subjects with congenital heart disease that has caused enlargement of the right side of the heart.

The Third Heart Sound in Emphysema

Clinical signs of cardiovascular changes are reported to be uncommon in emphysema. Parkinson and Hoyle (1937) said that simple clinical evidence that the heart was involved by the lung affection was usually wanting. Heart failure, although carefully sought with the aid of radioscopy in their series, was not common, and when it occurred it was a late event and almost invariably terminal.

I have looked for triple rhythm in patients with long standing emphysema and only discovered it in 5 (Fig. 17): in each case breathlessness from emphysema had been present for many years, but more recently heart failure with normal rhythm had set in, and with hepatic distension, ascites, and œdema in 3 of them. On auscultation in the mitral area triple rhythm,

Type Ib, was found, and the supernumerary sound was heard in the erect as well as in the reclining posture. Cardioscopy in these 5 patients showed cardiac enlargement and pulmonary congestion; the enlargement involved the right heart and pulmonary artery, and there was slight distension of the left ventricle although none had hypertension. The pulmonary artery index was 7·2, 8·0, 8·0, 8·2, and 9·5 in these five patients compared with an average of 6·2 in a control series of ten patients who had much emphysema without heart failure and presented a dual heart rhythm. In 80 patients with emphysema examined radiologically by

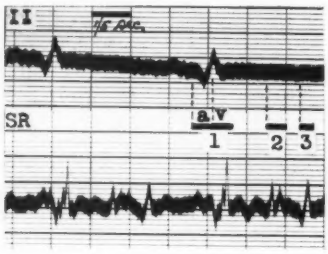


FIG. 16.—Triple rhythm, Type Ib, in a man, aged 71, with hypertensive heart failure.

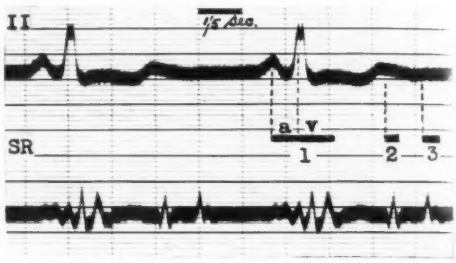


FIG. 17.—Triple rhythm, Type Ib, in a man, aged 58, with heart failure from emphysema.

Parkinson and Hoyle (1937), slight or moderate enlargement of the right auricle was present in 11, of the conus of the right ventricle in 33, and of the pulmonary artery in 22; a similar degree of enlargement of the right ventricle showed in 14 cases, but great enlargement was only met with in 4 patients, 3 of whom had heart failure.

Clinical and radiological examination of patients with emphysema permits me to say that triple rhythm, Type Ib, in these cases signifies prominent enlargement of the right heart and heart failure, and that it connotes the changes shown in Fig. 18. These changes were absent in patients with emphysema in whom a dual heart rhythm was heard (Fig. 19). This auscul-

FIG. 18.—Triple rhythm, Type Ib, in a man, aged 53, with heart failure from emphysema. Teleradiogram shows considerable cardiac enlargement and pulmonary congestion; pulmonary artery is distended with a P.A. index of 9·5.

FIG 19.—Dual rhythm in a woman, aged 42, with emphysema and bronchitis and without heart failure. Teleradiogram shows no cardiac enlargement and a P.A. index is 6·3.

tatory finding of triple rhythm in emphysema is, therefore, a sign of prognostic significance for it signifies that any patient presenting it is unlikely to survive many months. Four patients reported here died within five months of finding this form of triple rhythm, and the other is precariously ill. The same triple rhythm has since been found in patients with pulmonary embolism and pulmonary hypertension.

A triple rhythm was found in 5 patients with constricting pericarditis but it was absent in 13 others. As the cases showing triple rhythm were young subjects, a further study of this group is being made to try to discover any factor which might determine the presence of the third heart sound.

Type II.—Addition of the Fourth Heart Sound

Triple rhythm caused by an added sound in late diastole is not less important in diagnosis and prognosis than triple rhythm resulting from an extra sound in early diastole. Since the adventitious sound in this form occupies a place that is later than the point at which the third sound occurs it may be called the fourth sound, and it immediately precedes the first heart sound. Actually it occurs during auricular systole so that it only precedes the ventricular moiety of the first heart sound (Fig. 1). As in the case of triple rhythm of Type I, so also in this variety designated Type II, there are two classes; in the first the supernumerary sound is produced by auricular systole and appears only when auriculo-ventricular conduction is delayed; in the second, although the sound is produced in or by the left ventricle affected by failure, regulated contraction of the auricle is again necessary for its production, and it is never heard in auricular fibrillation. Among 60 patients with triple rhythm due to the presence of the fourth heart sound, 14 belonged to the first group and 46 to the second. These two varieties will now be described.

Type IIa.—The Fourth Heart Sound in Delayed A-V Conduction

A sound produced by auricular systole is easily recorded, but the circumstances deciding its audibility are not altogether understood. In sound tracings from 16 healthy schoolboys, Bridgman (1914) recorded a presystolic sound in 11 of them. Since it was represented by a wave that usually showed displacement in only one direction, he concluded that it was subject to marked damping at the source. The wave occurred 0·02 sec. after the beginning of the auricular wave of the apex cardiogram, 0·07 sec. before the beginning of the first sound, and lasted 0·04 sec. Bridgman suggested that the sound was produced by tension of the ventricular walls caused by the onset of auricular contraction, and that there was a possible relationship between this sound and presystolic gallop. Lewis (1915) explained that the auricular sounds were not heard in the normal heart because the auricular and ventricular systoles occurred too close together. He also said that when contraction of the auricle was audible in certain cases of heart block, the human ear could sometimes detect a double sound and that sound records illustrated its dual nature. Reid (1921) also observed two components in the auricular sound itself where the second promptly followed the first and the vibrations of the second filled the interval of 0·05 sec. before the onset of the sound due to ventricular systole. After introducing a sound recording device into the œsophagus in 50 normal subjects, Taquini and Braun-Menendez (1935) were able to see the auricular sound clearly in every tracing. In 100 healthy students Braun-Menendez and Orias (1934) recorded the auricular sound on the surface of the chest in 20, while Caeiro and Orias (1937) using a more sensitive device recorded auricular vibration in 17 out of 20 healthy young adults. Braun-Menendez (1938) said that although it was difficult to recognize the auricular sound by auscultation this did not mean that it was inaudible; the impression gained by auscultation was that of an impurity of the first sound, or when the auricular sound was louder, a splitting of the first sound.

In the interpretation of sound records taken simultaneously with the electrocardiogram it is an accepted fact that the first sound is never recorded earlier than the R wave. Any sound wave visible immediately in front of the R wave must be the direct or indirect result of auricular contraction. In 32 sound records from cases in which a clear first sound was elicited on clinical auscultation, an auricular sound was recorded graphically in 30. In 20 of these the sound commenced at the end of the P wave in the electrocardiogram and just after in 4, but in 6 it started earlier and coincided with the descending limb of P. In some instances of isolated auricular contraction as in complete heart block the auricular sound also commenced early and once coincided with the summit of the P wave when it showed two separate groups of vibrations which were appreciated by clinical auscultation, giving to the auricular sound a dual character (Fig. 20 and 21). Since the supernumerary sound in delayed auriculo-ventricular

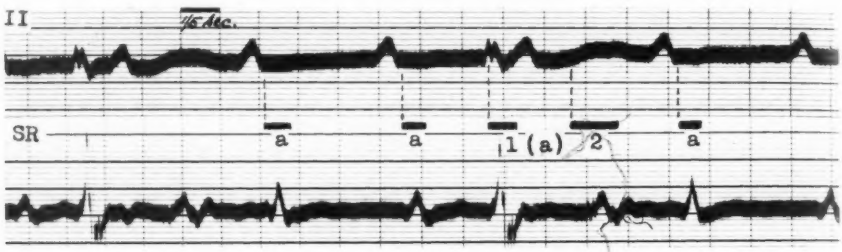


FIG. 20.—Auricular sounds recorded in complete heart block. Auricular wave immediately following the first heart sound (a) is suppressed.

conduction shows the same time relationship to the P wave as the auricular sound in records from subjects with dual rhythm, the sound is clearly caused by auricular contraction; it was never heard or recorded in auricular fibrillation. As in patients with complete heart block so also in subjects showing delayed A-V conduction the auricular sound is not always audible. In children and young adults the auricular sound was heard whenever the P–R interval in the electrocardiogram was prolonged, but not so in older subjects in whom it was often inaudible.

In the 14 subjects in this series where triple rhythm resulted from delayed A-V conduction (Fig. 22), the P–R interval measured from 0·20 to 0·33 with an average of 0·25 sec. Six of them were considered healthy after an examination that included cardioscopy, and the remaining 8 showed disease, this including mitral stenosis, coronary atheroma, and bundle branch block. Although a prolonged P–R interval was found in 7 patients presenting

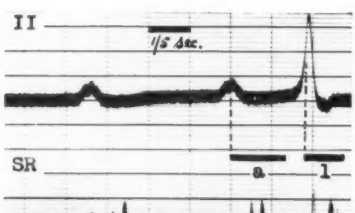


FIG. 21.—Isolated auricular sound in complete heart block showing early and late components; commencement coincides with summit of P wave. Tracings from a man, aged 60, with Stokes-Adams attacks. Auricular sound occasionally audible.

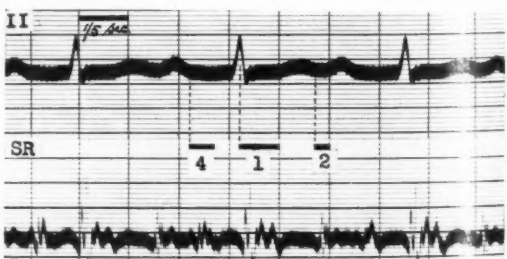


FIG. 22.—Triple rhythm. Type IIa, in a woman, aged 25, who showed no evidence of heart disease apart from delayed auriculo-ventricular conduction.

a fourth heart sound in left ventricular failure, it was not here regarded as having by itself initiated the supernumerary sound. Besides, the area over which the sound was heard was characteristic of the form of triple rhythm found in failure (Type IIb). Triple rhythm (Type IIa) was best heard a little internal to the mitral area and for a little distance around (Fig. 4). Although best heard with the subject reclining, it persisted in the erect posture. The rhythm was often made more obvious by induced tachycardia.

Sometimes four sounds could be heard in each cardiac cycle and the circumstances favouring this *quadruple rhythm* were found in the association of a delayed A-V conduction with a

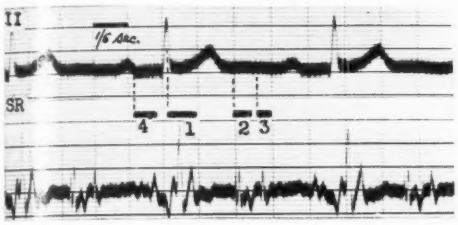


FIG. 23.—Quadruple rhythm caused by presence of fourth heart sound in delayed auriculo-ventricular conduction, and third heart sound in mitral stenosis, from a girl, aged 19.

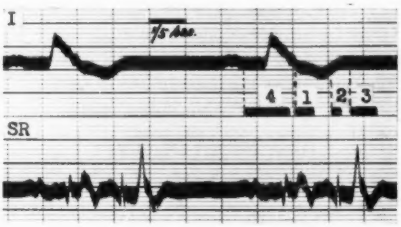


FIG. 24.—Quadruple rhythm caused by presence of fourth heart sound in delayed A-V conduction, and third heart sound in hypertensive failure, from a man, aged 44.

physiological third heart sound, or with a third heart sound in mitral stenosis (Fig. 23) or in prolonged hypertension (Fig. 24).

TYPE IIb.—THE FOURTH HEART SOUND IN LEFT VENTRICULAR FAILURE

For more than half a century this form of triple rhythm has been a physical sign familiar to many clinicians. There has been almost general agreement on its significance in diagnosis and in prognosis, and fair agreement on the mechanism of its production. Whenever opinion has been confused about its recognition it has usually meant that other varieties of triple rhythm have been included erroneously in this group rather than that a patient with this sound has been wrongly allocated to another group. Indeed, when a triple rhythm is alluded to as " gallop " without specific reference to its kind, it is understood as a rule to imply the type that is now to be described.

Among 60 patients with triple rhythm due to the presence of the fourth heart sound, left ventricular failure was the cause in 46, and the characteristics of this form have been determined from a clinical and graphic study of them. Hypertension had caused left ventricular failure in 41, and aortic incompetence, in 5. There were no cases of aortic stenosis.

The Fourth Heart Sound in Hypertension

As to the mechanism of this type of triple rhythm it is clear that two conditions are necessary for its production—left ventricular failure and a normally contracting auricle. Raised diastolic tension within the ventricle and increased intra-auricular pressure were mentioned by Mond and Oppenheimer (1929) as the cause of the supernumerary sound. Duchosal (1932) wrote that it was generally admitted that hypotonicity of the failing myocardium caused the ventricle to dilate suddenly and audibly under the influence of the auricular blood wave, so that auricular contraction on the one hand and ventricular hypotonicity on the other, were the two principal factors in the production of gallop rhythm. From his study of phonocardiograms Duchosal maintained that hypotonicity of the ventricle, which regulated the production and quality of the sound, could not by itself explain all the phenomena connected with gallop rhythm, and that it was necessary to consider the variation in the force and volume of the

auricular wave judged by changes in the interval between the P wave of the electrocardiogram and the supernumerary sound (the P–G interval). Since the sound appeared to come from the shock of the auricular blood wave on a hypotonic ventricle, he described it as auricular gallop, but Wolferth and Margolies (1933) considered the term misleading because there was no proof that the sound originated in the auricle.

Clinical features. The average age was 55 and only 3 were under the age of 40; this agrees with Bramwell's (1935) finding of 8 under 40 among 62 patients. Dyspnœa was always the outstanding symptom and in 30 this included cardiac asthma. Œdema of the ankles was found in 5 patients only and crepitations in the lungs or pleural effusion were present in less than half. In 38 the diastolic blood pressure was above 100, and the systolic was above 200 except in 6. In 3 patients a low blood pressure reading was ascribed to cardiac infarction. The cardiogram was usually abnormal and characteristic of hypertensive heart disease in that it showed left axis deviation, inversion of the T wave in lead I, and sometimes bundle branch block. Enlargement of the left ventricle, and sometimes of the other chambers in varying degree, was seen on cardioscopy. Pulmonary congestion, best seen at the hila, was also present in varying degree.

The supernumerary sound. The sound had a duller quality than the first heart sound which succeeded it. The interval separating the two sounds was brief, yet it was sometimes better appreciated by clinical auscultation than in the phonocardiogram where the sounds were often almost conjoined. It was usually heard along a line running from the displaced apex beat near the anterior axilla to the left border of the ziphisternum and was most intense at these two stations (Fig. 4). Thus among 41 patients it was heard at both places in 28, but better at the ziphisternum in 17 and at the apex in 11: in 8 it was heard at the apex only and in 5 at the xiphisternum only. I found no constant changes in the cardiac outline to correspond with the site of maximum intensity of the sound. Thèse findings differ from those of Wolferth and Margolies (1933) who stated that in most cases the gallop sound was heard best in the neighbourhood of the apex impulse and only occasionally over or just to the left of the lower end of the sternum. They also said that such right-sided gallop occurred with dilatation of the right side of the heart and tricuspid insufficiency. The characteristic dual impulse associated with this type of triple rhythm was felt in most cases and was invariably present whenever the supernumerary sound was heard well. This was best appreciated by placing the naked ear to the chest when the impulse could be felt and the sound heard at the same time. As with other forms of triple rhythm this sound was better heard with the patient in the reclining position although it persisted in the erect. French writers have written on the association of tachycardia with this type of triple rhythm, and Bramwell (1935) has emphasized it as a constant finding. Naturally, tachycardia is common in patients with hypertensive heart failure, but I found this rhythm in five patients with a normal heart rate, and failed to produce it in seven with hypertension and heart failure by inducing tachycardia by exercise or ingestion of trinitrin (1/50 grain). None the less, whenever the triple rhythm is heard faintly, tachycardia usually accentuates it, and this accentuation is sometimes due to the superimposing of the third on the fourth heart sound, the summation gallop of Wolferth and Margolies (1933), as a result of shortening of the diastolic period (Fig. 25). Lewis in 1915 spoke of the effects of auricular fibrillation on this type of gallop rhythm. He said that if the rhythm was the result of a sudden rush of blood into the ventricle at the time of auricular systole one would not expect to meet with it in cases of fibrillation, and he had never found it.

The sound record. That the interval between the fourth and first heart sounds in this form of triple rhythm may often be better appreciated on clinical auscultation than in a sound record, has already been mentioned. The clear presentation of this triple rhythm appears to depend more on the intensity of the fourth heart sound and less on the length of the interval between the fourth and first sounds, although this plays a part whenever it is obviously pro-

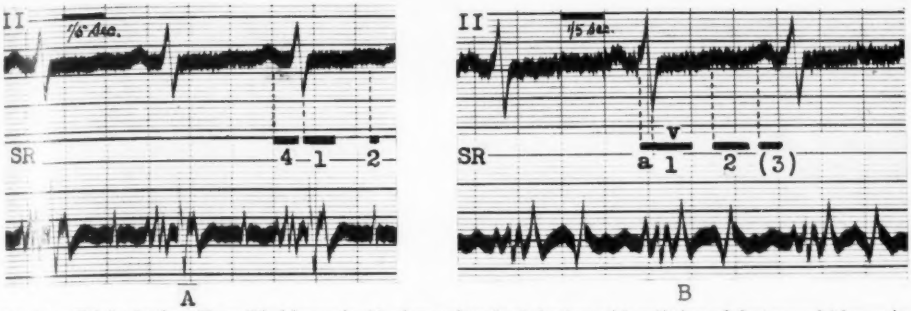


FIG. 25.—Triple rhythm, Type IIb (shown in A), changed to dual rhythm with splitting of first sound (shown in B), in a man, aged 69, with hypertensive heart failure, after treatment with rest and mercurial diuretics. The slower heart rate has caused separation of the third and fourth heart sounds. Third sound recorded but not audible.

lengthened. The intensity of the fourth sound probably depends on the degree of left ventricular failure; it is certainly increased by the frequent coincidence of the third sound which reinforces it. Duchosal (1932) has stressed the importance of the duration of the interval between the P wave in the electrocardiogram and the gallop sound in the sound record (the P–G interval). In connection with it he formulated two laws. The first law was that the P–G interval was an index of the seriousness of the affection; if the P–G was less than 0·05 sec. the prognosis was bad, but if greater the outlook was better. The second law was that the P–G interval varied in proportion to the improvement or aggravation of the case during the course of the illness. In cases presenting this triple rhythm, I have not found the start of the auricular sound in the phonocardiogram any nearer to the P wave of the electrocardiogram than in healthy subjects; it usually started at the end of the P wave as in the normal. Often when the start of the auricular sound wave appeared to coincide with the descending limb of the P wave or even with its summit—and such examples were common—it was found that the first part of the sound wave was the third heart sound which was continued into the fourth. When tachycardia subsided the third sound separated from the auricular sound which began at the end of the P wave. Although this summation effect of the third and fourth heart sounds is common in patients with left ventricular failure and tachycardia, I believe that the audibility of this type of triple rhythm depends a little on the summation effect but much more on the accentuation of the supernumerary sound itself from the ventricular failure.

The Fourth Heart sound in Aortic Incompetence

There were 5 examples of this, and left ventricular failure with normal heart rhythm was common to all of them. Hypertension was present in four and in one this was the result of coarctation of the aorta. Hypertension was absent in one case where the aortic leak developed quickly from bacterial endocarditis. With the progress of cardiac enlargement and failure in this patient, dual rhythm gave way to triple rhythm (Fig. 26). The clinical and graphic character of this supernumerary sound did not differ from that in hypertensive heart failure. It is likely that the fourth heart sound occurs as well in aortic stenosis and heart failure, but I have not yet met with a case.

Two conditions in particular have to be described in connection with triple rhythm, Type II: they are splitting of the first heart sound due to an accentuated but not displaced auricular sound, and splitting of the first sound in bundle branch block.

Splitting of the First Heart Sound

A splitting of the first sound results from a separation of its two natural sound components, the auricular and the ventricular. Although the designation of duplication may well convey

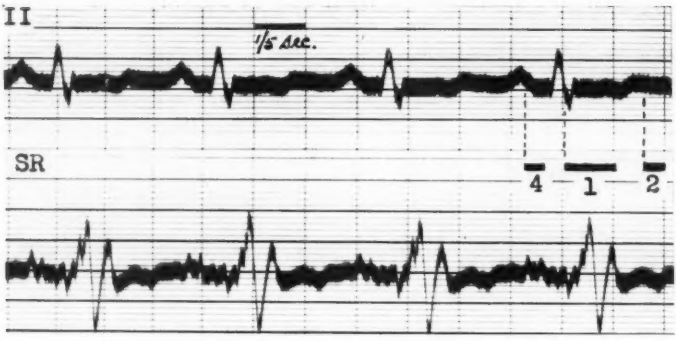


FIG. 25.—Triple rhythm, Type IIb, in a man, aged 62, with heart failure from aortic incompetence.

the impression gained by clinical auscultation, the term is a misnomer since the combined sound is never in fact repeated as a whole, but it often divides. It has been known for years that a " double first sound ", i.e. splitting of the first sound, was found in healthy subjects as well as in patients with heart disease. By itself this auscultatory finding has no special significance, except in bundle branch block which is to be considered separately, for it is only an exaggeration of the separation (and often in health) of these two constituent groups of vibrations. Cossio and Braun-Menendez (1935) found that in many cases where a diagnosis of splitting of the first sound had been made on clinical auscultation, the real cause of the auscultatory impression was the presence of an auricular sound. The frequency with which the auricular sound can be recorded phonocardiographically has already been mentioned, and it was found commonly in cases which showed neither splitting of the first sound nor the presence of a fourth heart sound. Usually only the second part of the auricular sound was evident and this was fused with the ventricular component of the first heart sound. A delay in auriculo-ventricular conduction (prolonged P–R interval), or bundle branch block, can each determine a splitting of the first sound, but a third variety of splitting is often heard in health and in the presence of a normal electrocardiogram, and the recognition of this is of great importance in clinical diagnosis. For this reason it is to be the subject of further cardiographic investigation.

Triple Rhythm in Bundle Branch Block

Lewis (1912 *b*) recorded the heart sounds in 4 patients with bundle branch block in whom a " duplication " of the first heart sound was heard on clinical auscultation. He said that the two sound elements could be dissimilar, in which case the first element was of smaller amplitude than the second and different from it in character. The first part commenced before, though the greater part of it coincided with, the ventricular complex. The second stood in much the same position as the normal first sound, but as a rule a little later, coming either 0·05 to 0·07 sec. after the opening of the electric deflections of the ventricle. The first element was properly speaking presystolic and occurred in part at least coincidentally with the auricular contraction; from its time relations it was clearly independent of ventricular systole. Lewis concluded that the double sound was not due to asynchronous action of the two ventricles resulting from the abnormal path taken by the contraction wave and leading to asynchronous closure of the valves. The P–R interval was prolonged in each of the two records that he published. From a clinical investigation of 41 cases of bundle branch block, Hill (1921) concluded that a duplicated mitral first sound was of little diagnostic value, because it occurred in cases other than bundle branch block and disappeared even while the block persisted. Campbell and Suzman (1932) reported an interesting case in which triple rhythm and bundle branch block disappeared simultaneously. Graybiel and Sprague (1933) described their

findings in 395 cases of bundle branch block; they said that diagnosis could only be made with certainty by the electrocardiograph. J. K. Lewis (1934) took sound records in 20 patients with bundle branch block; presystolic gallop was present in 9 and in 3 of these a presystolic impulse was felt; in 5 a duplicated first sound was heard. He came to the conclusion that the presence of triple rhythm in bundle branch block could be accounted for by the fact that both conditions occurred in the same general type of heart disease and under the same circumstances, and it was not related to the bundle branch block itself nor to asynchronism of the ventricles.

A triple rhythm was sought in 30 patients in whom a bundle branch block was shown in the electrocardiogram and it was found in 13. In 6 of these the triple rhythm was caused by the appearance of the fourth heart sound in delayed auriculo-ventricular conduction (Type IIa), and in the other 7 by the fourth heart sound in left ventricular failure (Type IIb). In only 2 of the remaining 17 cases with dual rhythm was the first sound clear in the mitral area; in 15 there was either a roughish systolic murmur with slurring of the sound sometimes simulating a presystolic murmur, or a splitting of the first sound. The relationship between a delayed auriculo-ventricular conduction time as shown by a prolonged P–R interval, and the incidence of triple rhythm in bundle branch block, was specially examined. A delay was present in 14 but not in the remaining 16. Out of the 14 cases with a P–R interval longer than 0·22 sec., 11 showed triple rhythm and 3 had dual rhythm. Among the 16 cases in which the P–R interval was less than 0·2 sec. there were 14 with dual rhythm. The remaining 2 showed triple rhythm (Type IIb) from left ventricular failure. These findings are summarized in Table V.

TABLE V

AUSCULTATORY FINDINGS IN 30 PATIENTS WITH BUNDLE BRANCH BLOCK

Incidence of triple rhythm			
Dual rhythm in 17	2—Clear first sound		
	15—Rough systolic murmur; slurred first sound; splitting of first sound		
Triple rhythm in 13	6—Type IIa		
	7—Type IIb		
Triple rhythm in relation to A-V period			
Prolonged P–R in 14 ..	3—Dual rhythm		
	11—Triple rhythm	6—Type IIa	
		5—Type IIb	
Normal P–R in 16	14—Dual rhythm		
	2—Triple rhythm (Type IIb)		

The ventricular part of the first sound in the phonocardiogram of bundle branch block appears in relation to an S wave that is delayed because of a lengthening of the R–S interval. When this is considered alongside the fact that the P–R interval is also full and often prolonged in this condition, it is not difficult to understand why splitting of the first sound is common in patients presenting bundle branch block (Fig. 27).

Thus in the series reported here a pure first heart sound was uncommon (only 2 out of 30).

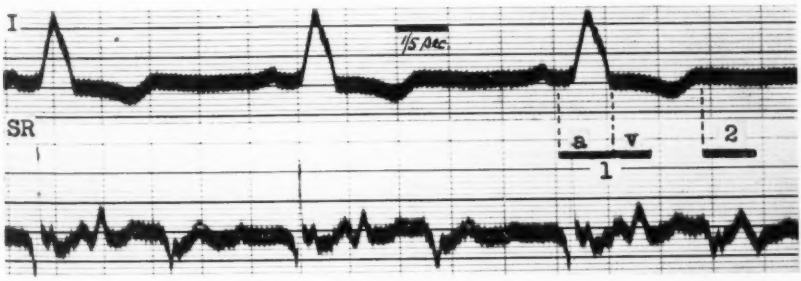


FIG. 27.—Spitting of first heart sound in bundle branch block in a man, aged 62. Auricular part of first heart sound is accentuated and ventricular part commences opposite delayed S wave of electrocardiogram.

In half the cases the sound was either obscured by a murmur or showed splitting. Triple rhythm in bundle branch block was never present unless there was delay in A-V conduction or left ventricular failure, and often both conditions existed together. It is because of this separation of the auricular and ventricular components of the first heart sound in bundle branch block that the condition may be referred to as one of " potential triple rhythm." The ease with which this rhythm becomes established either by a further slight increase in the P–R interval or at the first sign of left ventricular failure, is dependent on the already lengthened P–S interval which characterises bundle branch block.

Type III.—An Extra Heart Sound in Late Systole

Under the title systolic gallop, Johnston (1938) reported 21 patients in whom the systolic position of the supernumerary sound was shown in phonocardiograms. He pointed out that it usually happened in healthy hearts and that its importance lay in the fact that it was sometimes mistaken for a diastolic gallop. Laubry (1930) defined gallop rhythm as the result of the interposition of a third independent sound between the two heart sounds; it might occur during the short silence (systolic gallop) which was rare, or during the long silence (diastolic gallop) which was common and the only form which needed study. Among my 270 cases of triple rhythm there were 5 in which the supernumerary sound was situated in the systolic period. In all five a correct clinical interpretation was made before undertaking the phonocardiographic test which confirmed it (Fig. 28). Although casual auscultation may regard

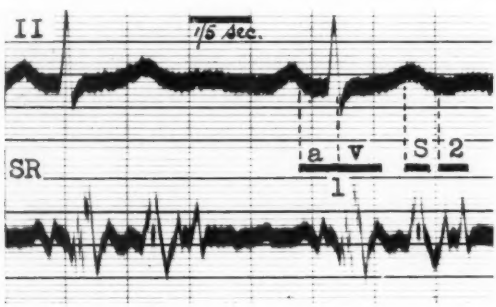


Fig. 28.—Triple rhythm, Type III, in a healthy man, aged 37. Added sounds are recorded in late systole and precede the second sound.

this as triple rhythm (Type I) a more careful examination will localize the supernumerary sound in front of and not after the second heart sound. It is possible to recognize the second of the three heart sounds as the supernumerary sound by paying attention to its character as well as its timing. Thus it can be made out that it is dull or muffled or like a click, compared with the clear second heart sound which immediately follows it. These characteristics were more readily appreciated when the stethoscope was moved away a little distance from the point of maximum intensity in the mitral area. In none of the five patients was there heart disease; in one the left ventricle was slightly enlarged from moderate hypertension. It is of interest that all five subjects had been informed after previous clinical examinations that they had " heart trouble," which shows that the importance of this innocent rhythm lies in its recognition.

Summary and Conclusions

Triple rhythm is the cadence produced by the recurrence in successive cardiac cycles of three separate sounds. The chief purpose of this work has been to classify triple rhythm in accord with findings on clinical, radiological, cardiographic, and sometimes pathological examination of the heart, in patients presenting this auscultatory sign. Splitting of the first

sound at the apex or of the second sound at the base of the heart are not included in its scope. The investigation has shown the need for discarding the terminology hitherto in use for triple rhythm and adopting one that is based on the clinical condition and avoids any preoccupation with the mechanism of the extra sound. As soon as it becomes the custom to listen specifically for a sound in addition to the more familiar first and second heart sounds, triple rhythm will be found to be common, perhaps as common as dual rhythm in patients sent for examination of the heart.

When the position of the adventitious sound in the cardiac cycle was considered alongside the clinical state of the patient in 270 cases with triple rhythm, it was possible to place them in three groups. As a rule, even under the handicap of fairly severe tachycardia, the position of the extra sound could be told by auscultation, aided by the clinical data, and before phonocardiography was used for scientific support.

In the first group (Type I), consisting of 205 cases, the added sound was the third heart sound occurring in early cardiac diastole. This group comprised of 125 healthy subjects, and 80 patients with right ventricular heart failure. The innocent triple rhythm (Type Ia) is distinguished from that due to right heart failure (Type Ib) by regarding the site of maximum audibility of the sound, the effect of posture upon the sound, and the health or disease of the heart. In Type Ia the sound is best heard a little internal to the normal apex in the mitral area, it is usually audible only in recumbency, and it is found in young healthy persons. It is uncommon after 24 (20 out of 125 in this series) and after 40 it is seldom if ever heard. On cardioscopy some degree of prominence of the pulmonary artery is a characteristic finding—an association in keeping with the common incidence of this auscultatory sign in children where a prominence of the pulmonary arc is a recognized feature of the normal radiogram. In Type Ib the sound is loudest at the apex, which is displaced according to the degree of cardiac enlargement; it persists in the upright as well as in the recumbent posture, and it is associated with disease that causes right ventricular enlargement and failure, such as mitral stenosis, hypertension, thyroid toxæmia, congenital heart disease, emphysema, pulmonary embolism, and pulmonary hypertension. Triple rhythm was present in half the cases of mitral stenosis and in four-fifths of those with auricular fibrillation. More often than not the third heart sound in mitral stenosis was joined with the characteristic diastolic murmur. When the third heart sound was present in hypertensive failure there was clinical evidence of failure of the right as well as of the left ventricle (biventricular failure), and cardioscopy showed enlargement of the right heart in addition to that of the left, and pulmonary congestion characteristic of the early phase of this failure. Patients with thyroid toxæmia showing a third heart sound had general enlargement of the heart and a prominent pulmonary artery; indeed the finding of this triple rhythm in each case predicted such changes while a series in which there was dual rhythm were without cardiac enlargement. Not all cases of congenital heart disease showed the third heart sound; but, when they did, enlargement of the right side of the heart, although probably not the only criterion, seemed essential to its appearance. The few patients with heart failure from emphysema, in whom considerable enlargement of the heart was seen at cardioscopy, showed this triple rhythm. A series of cases of emphysema with dual rhythm showed slight or no cardiac enlargement and no failure, so that the finding of the third heart sound in emphysema implies the presence of cardiac enlargement and failure and predicts a serious prognosis.

In the second group (Type II) the fourth heart sound is added during auricular systole and at the end of ventricular diastole. There were 60 patients with this variety of triple rhythm. In 14 of them it was the outcome of delayed A-V conduction (Type IIa). Not all cases whose P–R interval exceeds 0·2 sec. will show triple rhythm, although in young subjects, few will fail to present it. In 46 patients the extra sound appeared during left ventricular failure (Type IIb), where auricular action, although probably not the direct cause of the sound, is essential for its production, because it disappears with the onset of auricular fibrillation. Hypertension

is the usual cause of the left ventricular failure initiating this variety of triple rhythm, but occasionally it is the result of aortic incompetence. The added sound in these cases, although audible as a rule over the displaced apex beat, is usually best heard near the xiphisternum, and since it is accompanied by a palpable impulse, the rhythm is well appreciated by direct auscultation whereby the impulse is felt and the triple rhythm is heard simultaneously. This rhythm is often annulled when failure symptoms abate after the use of mercurial diuretics, but later it may give way to triple rhythm (Type Ib) when failure of the right heart has become added.

Bundle branch block with its wide P–R and QRS periods is a potential source of triple rhythm on this account for the fourth heart sound will appear when the P–R interval lengthens further or when the left ventricle begins to fail.

In the third, and least important group (Type III), an extra sound is added in late systole. It occurs in health, and almost its only importance lies in distinguishing it from the third heart sound. Since tachycardia is usually absent, its recognition on clinical auscultation is not difficult.

Triple rhythm is a common auscultatory sign, and it can be of great aid in the diagnosis of cardiovascular disorder. It should be sought specifically in every case, and when found, the position of the supernumerary sound in the cardiac cycle should be traced, and its significance determined in the light of clinical findings and in accordance with some classification such as that here proposed.

I wish to thank Dr. John Parkinson, Physician to the Cardiac Department, for his helpful criticism of this work. Mr. William Dicks, Technician to the Department has collaborated in producing the sound records.

References

Bramwell, C. (1935). *Quart. J. Med.*, **4,** 149.
Braun-Menendez, E. (1938). *Lancet*, **2,** 761.
—— and Orias, O. (1934). *Rev. Argent. Cardiol.*, **1,** 101.
Bridgman, E. W. (1915). *Heart*, **6,** 41.
Caeiro, A., and Orias, O. (1937). *Rev. Argent. Cardiol.*, **4,** 71.
Campbell, M., and Suzman, S. S. (1932). *Lancet*, **1,** 985.
Conner, L. A. (1927). *Amer. Heart J.*, **2,** 514.
Cossio, P., and Braun-Menendez, E. (1935), *ibid.*, **2,** 149.
Duchosal, P. (1932), *ibid.*, **7,** 613.
Einthoven, W. (1907). *Arch. ges. Physiol.*, **120,** 31.
Gibson, A. G. (1907). *Lancet*, **2,** 1380.
Graybiel, A., and Sprague, H. B. (1933). *Amer. J. Med. Sci.*, **185,** 395.
Gubergritz, M. (1925). *Ztsch. Klin. Med.*, **102,** 109.
Hill, I. G. W. (1931). *Quart. J. Med.*, **24,** 15.
Holt, E. (1927). *Amer. Heart J.*, **2,** 453.
Hirschfelder, A. D. (1907). *Bull. Johns Hopkins Hosp.*, **18,** 265.
Johnston, F. D. (1938). *Amer. Heart J.*, **15,** 221.
Laubry, C. (1930). *Nouveau Traité de Path. Int.*, Paris.
Lewis, J. K. (1934). *Arch. intern Med.*, **53,** 741.
Lewis, T. (1912). *Heart*, **4,** 241.
—— (1912). *Quart. J. Med.*, **6,** 441.
—— (1915). *Lectures on the Heart*, N. York.
—— (1934). *Diseases of the Heart*, London.
Lian, C. (1934). *Problèmes Actuels Path. Méd.*, **3,** 257.
Mond. H., and Oppenheimer, E. T. (1929). *Arch. intern. Med.*, **43,** 166.
Obrastzow, W. P. (1905). *Ztsch. Klin. Med.*, **57,** 70.
Parkinson, J., and Cookson, H. (1931). *Quar. J. Méd.*, **24,** 499.
—— and Hoyle, C. (1937). *Quar. J. Med.*, **30,** 59.
Potain, C. (1856). *Bull. Soc. Anat. de Paris*, **31,** 378.
—— (1866). *Bull. et Mem. Soc. Méd. des hôp. de Paris*, **3,** 138.
—— (1876). *Ibid.*, **12,** 137.
—— (1880). *Gaz. de hôp.*, **53,** 529.
—— (1894). *Clin. méd. de la Charité*, Paris, **29.**
—— (1900). *Semaine Méd.*, **20,** 175.
Reid, W. B. (1921). *J. Amer. Med. Assc.*, **76,** 928.
Sewall, H. (1909). *Amer. J. Med. Sci.*, **138,** 10.
Steinberg, L. D. (1925). *Z. Kinderheilk*, **40,** 620.
Stokes, W. E. (1855). *Diseases of Heart and Aorta*, Philadelphia.
Taquini, A. C., and Braun-Menendez, E. (1935). *C. R. Soc. Biol.*, Paris, **120,** 728.
Thayer, W. S. (1908). *Boston Med. Surg. Jour.*, **158,** 713.
—— (1909). *Arch. intern. Med.*, **6,** 297.
White, P. D. (1931). *Heart Disease*, N. York.
Wolferth, C. C., and Margolies, A. (1933). *Amer. Heart J.*, **8,** 441.

TREATMENT OF SUBACUTE INFECTIVE ENDOCARDITIS WITH HEPARIN AND CHEMOTHERAPY

BY

W. TREVOR COOKE AND A. BRIAN TAYLOR

From the Birmingham United Hospital

Received June 14, 1943

The incidence of bacterial endocarditis in rheumatic heart disease has been reported by various workers to be between 4 and 17 per cent, while in congenital heart disease it is between 14 and 22 per cent. The condition has been regarded by most physicians as uniformly fatal, though undoubtedly some mild and a few severe cases occasionally recover as Libman (1934) and Hamman (1937) have pointed out. By examining only reported series of cases of infective endocarditis treated by non-specific means, Lichtman and Bierman (1941) found that 6 out of 634 had undergone spontaneous cure. There are also reports of small epidemics of apparently proven cases in which the recovery rate has been high (Oille, Graham, and Detweiter, 1915, 1924, and Salus, 1920). Since the introduction of the sulphonamide drugs, there have been many reported cures and consequently a great revival of interest in the diagnosis and treatment of this condition. Having observed the successful cases reported by Kelson and White (1939) treated with sulphapyridine and heparin, we undertook this investigation, primarily to study the combined method of therapy with heparin and sulphonamides.

The lesion is a focus of relatively avirulent organisms enclosed in a mass of platelets and fibrin on a damaged valve. In 90–95 per cent of cases, the organisms are of the *Streptococcus viridans* type. The method by which they form these foci is debated: they may be embolic in the damaged valve or deposited on the surface with the platelet thrombi. Von Glahn and Pappenheimer (1935) have suggested that the lesions are grafted on to an active rheumatic endocarditis in most cases. The blood of these patients contains a very high antibody titre against the infecting organism and this factor alone tends to localize any transient bacteræmia. The platelet thrombi thus provide an ideal nidus for bacterial proliferation, providing as they do an excellent barrier from the bacteriocidal action of the blood, and situated upon a tissue that has the most sluggish reaction in the body, because there is minimal blood vessel and leucocyte invasion in the damaged valves. The infection is able to continue in the valve only if the deposition of fibrin exceeds the rate of invasion of leucocytes and it is upon this balance that the ultimate fate of the patient depends. Treatment will therefore depend upon either preventing the further deposition of fibrin or killing the organism by methods such as chemotherapy.

Heparin and Chemotherapy

Friedman, Hamburger, and Katz (1939) tried the first concept by using continuous intravenous heparin to bring about a prolongation of the clotting time during a period of two weeks or more and so slowing the deposition of fibrin. Since their original report some 5 cases at least have been treated and all have died. Kelson and White (1939) combined both concepts of treatment and reported 4 cases cured out of a total of 7 treated. This combined therapy has now been given to more than 70 reported cases of which 7 have survived. Such treatment, however, is not without danger. The risks of continuous intravenous therapy in

seriously ill patients for a period of fourteen days are considerable. The increased fluidity of the blood carries with it still more dangers. Cerebral hæmorrhage and cerebral emboli have been attributed to the prolonged clotting time, and Kleiber (1940) and Witts (1940) have reported renal hæmorrhage. All these complications can occur without any therapy, and it may be difficult to prove statistically that there is any increased risk in the use of heparin. In our Case 5, we considered that the patient's death was directly due to heparin. Prior to therapy his condition had been good, his clotting time had been markedly prolonged by heparin, and his temperature adequately controlled by sulphapyridine; and at autopsy the vegetation was small and suggested that healing was taking place: however, he died suddenly of cerebral hæmorrhage whilst under treatment. In most reported cases, fairly adequate prolongation of the clotting time was obtained. In four of our cases it seemed inadequate in spite of using the doses of heparin recommended. Some of the preparations used appeared to be lacking in potency (cf. Petch, 1940). It is difficult to believe, in the absence of experimental proof, that healing of the lesion could take place in the short space of two weeks. It is also fair comment that no case has yet been reported cured by the use of combined therapy in which complete control of the infection had not already been attained by chemotherapy alone, so that the role of heparin becomes extremely difficult to evaluate. At present, opinion is against the further use of heparin as now administered because the dangers appear to outweigh the uncertain advantages.

Case 1. A man, aged 22, was admitted complaining of cough, palpitation, and sweating of five weeks duration. On examination, he had mitral and aortic valvular disease, an enlarged spleen, petechiæ, and red cells in the urine. The blood culture was positive for *S. viridans*. His temperature varied between 101° and 102° F. He had a moderate degree of anæmia. Chemotherapy (sulphapyridine 45 g. during the first 13 days followed by 62 g. and prontosil 60 g. over the next 24 days) caused an immediate reduction of his temperature. On the seventh day, intravenous heparin in saline was given (750,000 units in 10 pints normal saline over seven days). No definite effect upon the clotting time was noted. He died five weeks after this and two weeks after stopping chemotherapy, in congestive failure. There was no autopsy.

No adequate deductions can be made from this case. He probably died from rheumatic carditis with the infective process temporarily controlled by the chemotherapy. There does not appear to be any evidence that the heparin played any role in the maintaining of normal temperatures or indeed that it exerted any action at all in the dosage given. The extra fluid may have played some part in the subsequent congestive failure. A normal temperature is not infrequently seen in the terminal stages of this disease.

Case 2. A man, aged 30, was admitted on 13/10/39 complaining of pyrexial attacks and general malaise following dental extraction five months previously. Examination showed a good general condition, clubbed fingers, and signs in the heart of a patent ductus arteriosus. Blood cultures grew *S. viridans*. The temperature varied between 97 and 101° F. After two short trials of chemotherapy with immediate control of the pyrexia, sulphapyridine was given for one month. Blood cultures became negative immediately and on the ninth day, intravenous heparin in saline (1·6 g. in 23 pints of saline in 10 days) was given. Only slight prolongation of the clotting time, from 5 to 15 minutes, was obtained. The temperature remained normal for eight weeks apart from one episode of chest pain suggestive of a pulmonary embolus. Following a severe hæmolytic streptococcal throat, he again began to run a high temperature. Prolonged chemotherapy (101 g. over five weeks) again brought about a remission. During this period the remainder of his septic teeth were extracted and a number of blood cultures were negative. The patient felt well and had put on weight whilst his blood count had risen to over four million. He left hospital in May, 1940.

Nothing further was seen of him in spite of repeated requests until he was again readmitted. He had worked for six months on a light job, but two months prior to admission, had had a recurrence of all his previous symptoms. Examination showed the typical café-au-lait colour, splenomegaly, and Osler's nodes, while the heart showed in addition to the original lesion, signs suggesting involvement of the aortic and the mitral valves. Blood cultures were again positive for *S. viridans* and the pyrexia varied between 99–101° F. Chemotherapy was again started and 150 g. sulphapyridine were administered over 45 days. The temperature was fairly well controlled on this regime, only occasional temperatures of 99–100° being observed: the white cells were not depressed in spite of a moderate degree of anæmia (2·6 million). At first it seemed that a further remission would be induced, but after four weeks his condition began to deteriorate and chemotherapy was subsequently

stopped. He was discharged home and died three days later, about two years after the onset of his illness. There was no autopsy.

Here, the onset appeared to be precipitated by his dental extractions and the source of the infection may have been there. Sulphapyridine was probably the main factor in producing the good remission that he had early in his illness. Heparin had very little part and very little effect in prolonging the clotting time. In addition to his congenital heart lesion, he presented symptoms and signs suggestive of active rheumatism, involving the heart and especially the aortic valves. If such was the case, he was probably more liable to a flare up of the infective process. We considered that this patient's life was prolonged by the treatment.

Case 3. A girl, aged 19, was admitted 27/3/40, complaining of shortness of breath and swelling of her joints. Examination showed petechiæ, a mitral systolic murmur and thrill, and an early diastolic murmur at the aortic area. Her temperature varied between 101 and 103° F. Blood cultures were positive for *S. viridans*. Sulphapyridine brought about an immediate reduction in her temperature and after 40 g. had been given, it was discontinued, with an immediate reversion of her temperature to the previous levels. One week later, chemotherapy was again instituted and again the temperature was controlled. After 50 g. had been given over 9 days, the white cells fell to 400. She reacted well to blood transfusions and the fortuitous occurrence of an abscess of the buttock. Following her recovery, her condition remained unchanged for the next five weeks. A further 32 g. was given without any ill effects upon the white cells but after five days, the pyrexia reappeared. A further course of 16 g. had no effect at all upon the temperature. On 12/7/40, chemotherapy was again started in adequate doses with control of the temperature, and on the seventh day intravenous heparin in normal saline was given (2·25 g. in 15 pints of normal saline over 150 hours). On the third day, however, splenic infarction occurred, and the following day she developed signs at the left base with recurrence of temperature and general deterioration; heparin was accordingly stopped. Chemotherapy was continued for two further periods, 51 and 70 g. being given, with only slight control of the temperature. Her condition during this period deteriorated only slowly. Eventually five months after admission she went into coma and died, having during this time received 270 g. of sulphapyridine.

Autopsy showed numerous infarcts in lungs, kidneys, and brain. The heart weighed 560 g. with extensive vegetations on the mitral, aortic, and tricuspid valves.

Chemotherapy may have played a part in prolonging the life of this patient. Heparin had no effect except in the possible production of emboli. Again one failed to effect adequate prolongation of the clotting time with the doses of heparin that were given. Following agranulocytosis, further chemotherapy was not given without trepidation, but there was no reduction of the white cells in spite of the full doses of sulphapyridine, 182 g. in all. At first the organism seemed to be susceptible to the drug but eventually became resistant. The experience in this case made us persevere with more continuous chemotherapy.

Case 4. A man, aged 41. Eight months previously he had begun to run intermittent temperatures following a sore throat, gradually losing weight and developing malaise. He had had numerous small hæmoptyses. For the past five months he had been continuously in bed. Examination showed a very ill man with signs of aortic and mitral disease, splenomegaly, clubbed fingers, and a high swinging temperature. Blood cultures were positive for *S. viridans*. Whilst in hospital, he had a number of attacks of paroxysmal auricular fibrillation. His temperature responded immediately to chemotherapy and on the sixth day intravenous heparin and saline was started (1·5 g. in 4 pints of normal saline over six days). No prolongation of clotting time beyond 21 minutes was obtained, his normal being four minutes. On this therapy he deteriorated rapidly and began to run a temperature. He was allowed home, still taking sulphapyridine, and died a few days later. There was no autopsy.

This patient was already seriously ill when therapy was started and his course did not appear to be influenced in any way.

Case 5. A man, aged 36, was admitted, complaining of pyrexial attacks and malaise following dental extraction four months previously. Examination showed a mitral systolic murmur and thrill, finger clubbing, petechiæ, and splenomegaly. Blood cultures were positive for *S. viridans*. His temperature varied between 99 and 101° F. In spite of these findings, his general condition was good. Sulphapyridine was started with an immediate reduction of temperature. Owing to nausea and vomiting, a concentration greater than 9·9 mg. per 100 c.c. was never attained, the average being about 5 mg. On the seventh day heparin in saline was given intravenously (8·25 g. in 16 pints over 13 days). Satisfactory prolongation of the clotting times was achieved, up to 60 minutes.

There was an immediate rise of temperature with the intravenous therapy which settled again in two days. His blood count fell from four million to two and a half, and his condition which had been good began to deteriorate rather rapidly. He died suddenly from cerebral hæmorrhage on the thirteenth day of intravenous therapy.

Autopsy showed extensive cerebral hæmorrhage with previous emboli and extensive retroperitoneal hæmorrhage. The heart showed a small vegetation on the mitral valve less than ¼ inch long. Microscopical section of the valve and vegetation showed much fibroblastic activity and giant cell formation.

We considered that the death of this patient was almost directly due to heparin therapy and that had chemotherapy alone been employed, he would have had an excellent chance of surviving. As a consequence of the experience of this and the other cases, we were reluctant to submit further patients to the combined therapy before we had made an extensive trial of chemotherapy alone.

Chemotherapy Only

The second aspect of therapy is that of exerting bacteriostatic or bacteriocidal influences upon the organisms themselves. Innumerable substances have been administered by mouth, subcutaneously, and intramuscularly, without any effect until the sulphonamide group of compounds was tried, though Osgood (1942) has recently claimed good results from a modified treatment with neoarsphenamine. Experimentally it is difficult to show how the sulphonamides have produced these cures. Friedman (1941) has shown that sulphapyridine has little penetrating power into the fibrin barrier round the focus of bacteria. He reported unsuccessful results in 12 cases and concluded as a result of his experimental and clinical findings that chemotherapy was of no avail. Duncan and Faulkner (1941) confirmed these experimental findings but they showed in addition, that the sulphonamide derivatives would be included in the clot if they were given prior to the formation of the clot. The number of reported cures supports this observation and should refute Friedman's statement and Katz (1941) belief that no case has ever been cured by chemotherapy. Since the bacteriocidal power of the blood is already adequate to deal with any organism liberated but not with the source of the organisms themselves, the suggestion put forward by Duncan and Faulkner that the drugs act by being incorporated in the clot seems to be the most logical and probable mechanism.

Lichtman and Bierman (1941) found that 12 out of 200 reported cases of subacute infective endocarditis had recovered. They also pointed out that of 45 cases treated with hyperpyrexia in addition, 9 recovered. Such figures, though not dramatic and probably from rather selected series with milder cases, do offer some improvement upon the era before chemotherapy. Indeed, Graybiel and White (1942) suggest that it is now probable that one case in twenty recovers.

During the past three years, we have observed 20 cases (including the 5 to whom heparin was also given) to whom the sulphonamide group of derivatives was given in adequate doses. Of these, 5 were totally unresponsive to either sulphathiazole, sulphapyridine, or sulphonamide; 12 cases were moderately controlled with temporary antipyretic effect, and 3 showed complete remission of the pyrexia. Case 1 received sulphonamide for 37 days apparently with complete control of the infection before dying of congestive failure. It is difficult, however, to draw any conclusions from this case. Case 6 was completely relieved of his symptoms but died a year after the onset of his infection, with congestive heart failure. Case 7 has now been apyrexial for seven months and has had a normal sedimentation rate for five months.

Case 6. A man, aged 21, was admitted complaining of general malaise and high temperature for 13 weeks. He had had chorea when 4 and probably acute rheumatism when 18. He had been otherwise well and active.

Examination showed a pale but fairly well-built man with early finger clubbing. There was a systolic murmur at the apex and a marked musical diastolic murmur at the base. The tip of the spleen was just palpable. There was no petechiæ. Three blood cultures were negative. An X-ray examination of the heart did not show any enlargement.

For the first ten days in hospital he ran an irregular temperature to 102° F. With the administration of sulphapyridine (6 g. daily), the temperature fell to normal on the third day. For the next 8 months, only on three occasions did the temperature reach 99° F. Four days after starting therapy, he developed pain in the left hypochondrium and the spleen became more easily palpable. This disappeared after two days and was not felt again. After one month, the dose of sulphapyridine was halved to 3 g. daily and this dosage was continued for seven months, a total of 730 g. being given without any nauseating or obviously deleterious effects.

The sedimentation rate fell from 38 mm. per hour (Westergren) on starting therapy to 6 mm. per hour after six weeks and remained below this until his final illness.

His blood count gradually rose to 4,700,000 red cells (from 4·1), to 94 per cent hæmoglobin (from 80), and to 7500 white cells. His white blood cells count fell to 4900 on one occasion, but usually remained between 5500 and 6000, the polymorphs averaging 60 per cent.

He was discharged from hospital for further convalescence 14 weeks after admission. The only

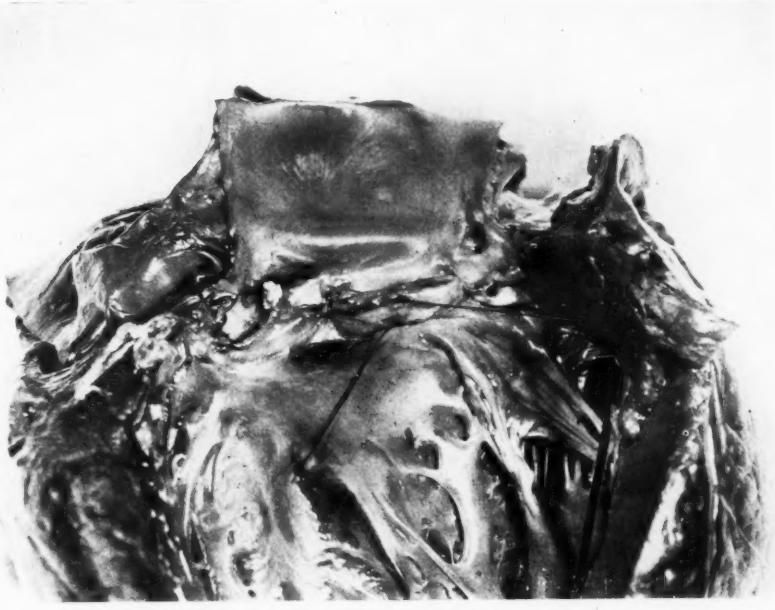
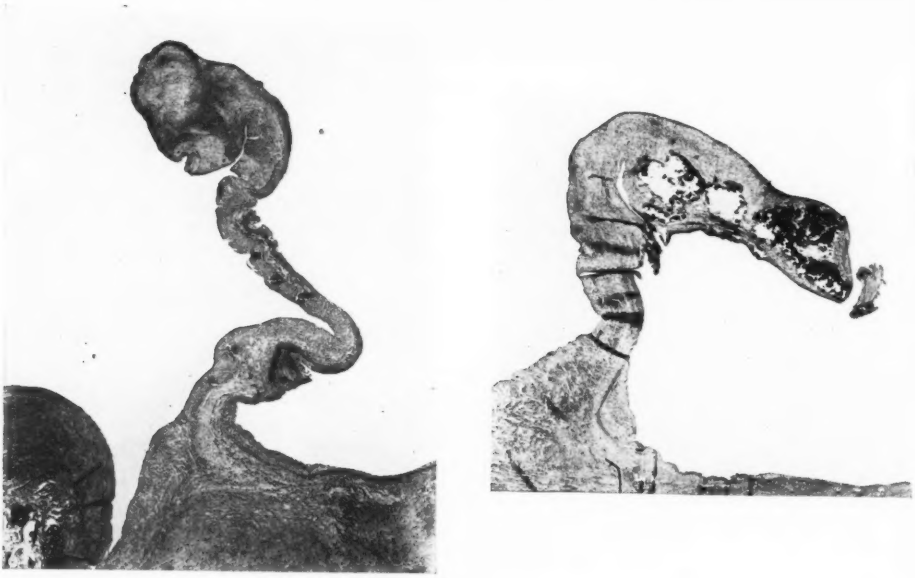


FIG. 1.—Interior of the left ventricle showing the aortic valves with two perforations, through which fibres have been passed. The endocardium round these perforations is well healed. The calcified vegetation is seen on the adjacent cusp. All three cusps show evidence of chronic rheumatic endocarditis.

disquieting feature was mild anginal pain on exertion, and a rapid pulse rate varying between 95 and 100. Over the next few months, he was seen regularly and it was noted that his heart was gradually enlarging. In spite of this, he felt well and was able to start work for a few hours daily as a laboratory technician. Unfortunately at the end of his first week he developed a severe cold and sore throat. Two weeks later he was readmitted with congestive failure, marked jaundice, and signs of consolidation at both bases. He died three days after admission.

Autopsy. Pleural cavities, a large amount of straw-coloured fluid. Lungs, both congested and œdematous with diffuse bilateral bronchopneumonia. Heart, enlarged and dilated, weighing 590 g. Left auricle, normal; left ventricle hypertrophied and dilated, with incompetence of the mitral valve and some thickening and shortening of the chordæ tendinæ. Aortic valve (Fig. 1) incompetent, the edges thickened. On edge of right cusp a pedunculated and calcified vegetation. Left cusp, two small perforations with healthy endocardium round them. Right ventricle, dilated and hypertrophied; right auricle, normal. Liver, congested. No evidence of perisplenitis or old infarcts in the spleen. Kidneys, a few typical healed scars of old infarcts.

Microscopical examination. Heart muscle showed considerable interstitial fibrosis. No Aschoff's bodies were seen. Sections through the calcified vegetation showed complete covering with endocardium (Fig. 2 and 3) with no evidence of any bacteria or inflammatory reaction. Sections through the two perforations of the valves also confirmed the diagnosis of healed infective endocarditis. Sections of the lungs showed diffuse bronchopneumonia with polymorphonuclear infiltration. The kidneys appeared to be normal except for the signs of congestion.



A B

FIG. 2.—(A) Section through the central cusp passing through the edge of the two perforations. Magnification ×11·7. (B) Section through the base of the calcified vegetation and the valve cusp, showing the extensive calcification. Magnification ×10·8.

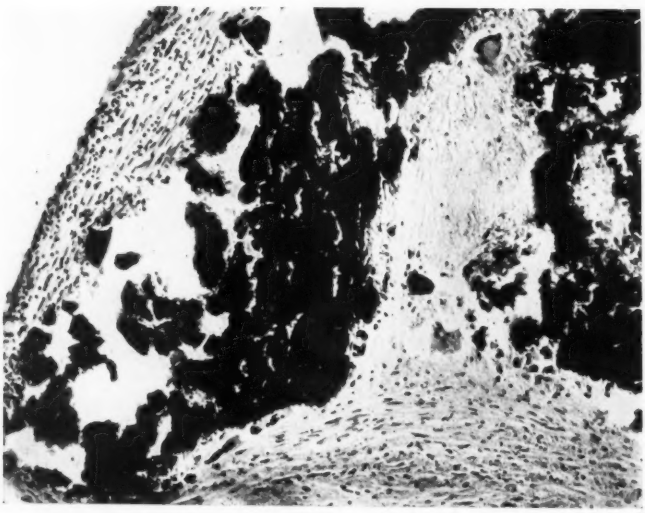


FIG. 3.—Section as in (B) showing the tip under high power. A number of foreign body giant cells can be seen round the edge of the calcification. There is a good endocardial covering and no evidence of any polymorphonuclear or lymphocytic infiltration in the extensive fibrous tissue. Magnification ×100.

This patient was able to take over 700 g. of sulphapyridine during seven months of therapy, showing no obvious deleterious effect and maintaining a good appetite the whole of the time. Examination of the sections of the heart valves showed that he had indeed been cured, but that the damage wrought upon the aortic valve had thrown too great a strain upon the myocardium and caused his death. This possibility is always present, so that even though the infection is cured, the residual lesion may be sufficient to kill the patient or cause him to be a permanent invalid. There are, however, an adequate number of reported cured cases who are earning their living, enough to indicate that the majority do attain a fair degree of recovery. There was no evidence of myocarditis in the sections such as has been reported by French and Weller (1942) following the use of the sulphonamide drugs.

Case 7. A milk-roundsman, aged 29, was admitted to hospital, complaining of pain in the left side and in the back of two weeks' duration. He had had rheumatic fever at the age of 18 for fifteen weeks, since followed by intermittent pains and swelling of his joints. Over the previous ten months he had noticed some shortness of breath and lassitude, insufficient, however, to keep him from his work. Ten weeks prior to admission, he had severe pain in his back for four days. Four weeks later, he had a severe cold and sore throat. Following this, he had severe soaking night sweats and began to feel really ill. Two weeks prior to admission, he again developed pain in the back and left loin which persisted until admission.

Examination showed a fairly well built man with a slight café-au-lait coloration, marked finger clubbing, and slight clubbing of the toes. There were no nodules or petechiæ. His teeth were grossly infected and carious. The heart was not enlarged. The mitral first sound was accentuated with a loud rough systolic murmur and thrill and soft mid-diastolic murmur. The sounds at the aortic area were normal. His blood pressure was 120/85. The spleen was just palpable. The urine contained a cloud of albumen, fatty and hyaline casts, and occasional red cells. His blood count was red cells 4,320,000 hæmoglobin 78 per cent and white cells 9150 with 75 per cent polymorphonuclears. The blood cultures showed 12 and 5 colonies per c.c. of *S. viridans*. His sedimentation rate was 81 mm. per hour (Westergren method). His temperature varied between 98° and 102° F. On commencing sulphapyridine (6 g. daily), his temperature fell to 99° F. As a normal temperature had not been produced in nine days, three injections of intravenous T.A.B. vaccine was given on alternate days. Following a moderately good reaction, his temperature became normal and has remained normal since except for three further T.A.B. injections given six weeks later. Slight nausea but no vomiting was produced by the sulphapyridine during the first five days, but thereafter he was able to take the drugs without any discomfort. After ten days, the dosage was reduced to 4 g. daily and on this dosage he maintained a blood stream concentration of sulphapyridine varying between 14 and 21 mg. per 100 c.c. His white cells never fell below 8500, his average count being 10,000 with 55 per cent polymorphs. His septic teeth were extracted in the sixth week of therapy and he was allowed to sit out of bed at the end of the ninth week. At this stage his pulse varied between 90 and 100 beats per minute while his sedimentation rate had dropped to 6 mm. per hour.

He was finally discharged at the end of his fourteenth week of therapy to a convalescent home, having put on two stone in weight whilst in hospital. Sulphapyridine was continued with two grams daily for a further four weeks. In all he took 400 g. of sulphapyridine without any ill effects. At present, he looks extremely fit, has some dyspnœa on moderate exertion, but is without any signs of bacterial endocarditis and his sedimentation rate is normal.

This patient appears to have attained a complete remission from his infection. He is still limited in his activities by his mitral stenosis. The consistently high blood levels of sulphapyridine may have played some part in his recovery. It was also of interest to note that his temperature only fell to normal after intravenous T.A.B. vaccine as advocated by Soloman (1941). We are not, however, inclined to attribute any definite role to this treatment as a factor in his recovery. At no time during chemotherapy did we experience any anxiety about the effect upon the white cells or kidneys.

Of the twelve cases that made some response to chemotherapy, all eventually became resistant and died. None of them took the drugs without showing much nausea, necessitating discontinuance of therapy in some cases even though there seemed to be some control of the infection. These toxic manifestations are the chief difficulty in the treatment and frequently prevent adequate concentration of the drug in the blood stream. One of these cases received sulphapyridine, sulphadiazine, and sulphathiazole in succession, 340 g. in all over nine weeks without a successful result although the temperature was fairly well controlled. There was,

however, much nausea and intolerance to the drugs and concentration above 6 mg. per 100 c.c. was not attained. In such cases, even if there is not complete control of the infection, it is felt that prolonged therapy is justified in view of the experience reported by Heyman (1940) in which some weeks elapsed before the patient became afebrile and eventually obtained a complete cure.

Agranulocytosis was encountered once (Case 2) but this responded well to therapy. Subsequent chemotherapy was controlled by white cell counts on alternate days, the leucocytes remaining consistently between 7000 and 10,000. Only a few cases of agranulocytosis have been reported, e.g. Leach *et al.* (1941) and Rinkoff and Spring (1941). Smith, Sauls, and Stone (1942) gave 894 g. of sulphanilamide in 73 days of continuous therapy to one of their patients who had been fit and well at the time of the report for 29 months. Thomas (1942) in considering the dangers of agranulocytosis in prolonged therapy in the prophylaxis of rheumatic fever, pointed out that in no instance had any toxic effects been seen after the first few weeks of treatment and that agranulocytosis had never been observed after the fiftieth day of chemotherapy given for any condition. We agree that the risks of chemotherapy are slight and in view of the seriousness of the disease being treated, that they may be neglected though routine weekly counts should be made.

In an effort to minimize the nauseating effect of the drugs, they have been administered in a mixture containing sulphapyridine or its equivalent 1 g., citric acid ½ g., nicotinic acid 25 mg., mucilage q.s., aq. menth. pip. ad. ½ oz. For the first few weeks of therapy, this was always given with food or milk. Ascorbic acid 300 mg. daily was also given in some cases including Cases 6 and 7, primarily to counteract the deficiency induced by any prolonged infection. Recently, however, Thompson (1942) has shown that ascorbic acid under experimental conditions markedly diminishes the toxic effects of sulphapyridine probably through its oxidizing properties. Vitamin A, 5000 units, and Vitamin D, 1000 units, were also administered daily to most patients.

The persistence of a slight temperature in some cases may well be due to the presence of active rheumatic fever. It is important therefore that prolonged rest in bed should be employed in any case where it seems likely that cure is probable, in order to allow the heart to recover as fully as possible from the serious infection to which it has been subjected. Even so, as we have pointed out above, the case may proceed to a fatal termination as in Kelson and White's Case 1 and our Case 6. Occasionally, as Jones and Bland (1939) have pointed out, the sulphonamide drugs may cause a fatal relapse in rheumatic myocarditis. The temperature may also be due partly to the drug itself. In one of our cases which eventually died and in Case 4 of Leach *et al*. this appeared to be so.

The evaluation of any therapy in infective endocarditis is made difficult by the uncertainties of diagnosis. In a patient with pyrexia, the presence of three out of four criteria, a valvular murmur, splenomegaly, positive blood cultures, or embolic phenomena, are usually accepted as sufficient evidence. The only absolute proof, however, is the presence of the lesion at autopsy. The diagnosis in Case 6 was confirmed at autopsy and Case 7 showed all four of the criteria usually accepted for the diagnosis. In early or mild cases, these criteria may not be fulfilled, and in such cases with recovery, cure cannot be claimed. These difficulties were well illustrated by one further case.

A woman, aged 26, was admitted with repeated hæmoptyses and slight pyrexia. Examination showed a pale sweating woman with signs of mitral stenosis. Whilst under observation she had repeated episodes of chest pain and hæmoptysis, and began to run a high swinging temperature. At the same time, she developed an aortic diastolic murmur and a collapsing pulse. Repeated blood cultures were negative. She showed no response to salicylates. Some control of the temperature was obtained with sulphthiazole, but after 45 g. had been given as her condition appeared to be deteriorating, she was taken home by her relatives. Now, 15 months later, she has a normal temperature but still an occasional hæmoptysis. The diagnosis of infective endocarditis therefore has been revised and it is considered that acute rheumatic carditis explained the whole illness.

Summary and Conclusions

Five cases were treated with combined chemotherapy and intravenous heparin. All died, and in one this was probably due to the heparin therapy.

Twenty cases (including the five treated with heparin) were studied under treatment with sulphonamide derivatives. Five were totally unresponsive, twelve were moderately controlled. Life was prolonged in some but all eventually died. Three cases became apyrexial; one died after 45 days of normal temperature, but as there was no autopsy, neither the diagnosis nor the state of the lesion could be determined. A second died one year after the onset of his infection and eight months after the control of his pyrexia by sulphapyridine: autopsy showed healed lesions of infective endocarditis. The third is well and working at his occupation as a milk-roundsman, at the present time, now twelve months after his discharge from hospital.

Intravenous heparin did not prove of value in our cases and, as others have found, should not be used in these cases.

Prolonged chemotherapy offers a chance of cure to a few patients though the great majority will not be so benefited. The dangers of such prolonged therapy are small and should not weigh against the chances of a successful outcome.

We wish to thank the Physicians of the Birmingham United Hospital for permission to study these cases. The cost of heparin was defrayed by a grant from the Medical Research Council.

References

Duncan, C. N., and Faulkner, J. M. (1940). *Amer. J. med. Sci.*, **200,** 492.
Friedman, M. (1941). *Arch. intern. Med.*, **67,** 921.
Friedman, M., Hamburger, W. W., and Katz, L. N. (1939). *J. Amer. med. Ass.*, **113,** 1702.
Hamman, L. (1937). *Ann. intern. Med.*, **11,** 175.
Heyman, J. (1940). *J. Amer. med. Ass.*, **114,** 2373.
Jones, T. D., and Bland, E. F. (1939). *Personal Communication.*
Katz, L. N. (1942). *Arch. intern. Med.*, **69,** 746.
Kelson, S. R., and White, P. D. (1939). *J. Amer. med. Ass.*, **113,** 1700.
Kleiber, E. E. (1940). *Ibid.*, **115,** 1713.
Leach, C. E., Faulkner, J. M., Duncan, C. N., McGinn, S., Porter, R. R., and White, P. D. (1941). *Ibid.*, **117,** 1345.
Libman, E. (1934). *Modern Concepts of Cardiovascular Disease*, **3,** 6.
Lichtman, S. S., and Bierman, W. (1941). *J. Amer. med. Ass.*, **116,** 286.
Oille, J. A., Graham, D., and Detweiter, H. K. (1915). *Trans. Ass. Amer. Phys.*, **30,** 674.
—— (1924). *Ibid.*, **39,** 227.
Osgood, E. E. (1942). *Arch. intern. Med.*, **69,** 746.
Petch, C. P. (1940). *Lancet*, **2,** 637.
Rinkoff, S. S., and Spring, M. (1941). *Ann. intern. Med.*, **15,** 89.
Salus, G. (1920). *Med. Klin. Berl.*, **16,** 1107.
Smith, C., Sauls, H. C., and Stone, C. F. (1942). *J. Amer. med. Ass.*, **119,** 478.
Thomas, C. (1942). *Bull. N. Y. Acad. Med.*, **18,** 508.
Thompson, M. R. (1942). *Arch. intern. Med.*, **69,** 662.
Von Glahn, W. C., and Pappenheimer, A. M. (1935). *Ibid.*, **55,** 175.
Witts, L. J. (1940). *Brit. med. J.*, **1,** 484.

PROCEEDINGS OF THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

The SEVENTH ANNUAL GENERAL MEETING of the Cardiac Society of Great Britain and Ireland was held at St. Thomas' Hospital, London, on Friday, June 11, 1943.

CHAIRMAN: SIR MAURICE CASSIDY

The Chairman took the chair at 10.15 a.m.
52 Members, 12 Temporary Members, and 2 Visitors were present.

PRIVATE BUSINESS.

1. The minutes of the last meeting having been printed in the Journal were confirmed and signed.

2. The accounts, audited by Donald Hall and Chamberlain, were presented by the Council and approved, the balance being £43 6*s.* 11*d.* The Council had decided that no subscriptions should be collected for the year 1943/4.

3. The following new Members were elected:—

Ordinary Members	*Associate Members*
Hugh Barber	W. Trevor Cooke
A. G. Biggam	Alastair Hunter
Athelstane Hill	E. V. Sharpey-Schafer
B. A. McSwiney	W. K. Stewart

Seven associate members were re-elected for another period of three years.

4. Leslie Cole, Cambridge, and John Parkinson, London, were elected members of the Council for the years 1943–47.

5. The Secretary was re-appointed for another year, and William Evans was again asked to act as Assistant Secretary.

6. The Secretary reported as follows.
   (*a*) He had learnt with pleasure from a letter from America that Charles Laubry, whose obituary notice had been published in the Journal, was still alive and in good health.
   (*b*) The Committee appointed to report on the scheme for the treatment of juvenile rheumatism had submitted their report, which would be dealt with by Bruce Perry later in the discussions; and the Council had instructed the Secretary to get in touch with the Pædiatric Association, who had drawn up a similar report, to see if it was possible for the two bodies to issue a joint report.
   (*c*) The Council had asked Cassidy, Chamberlain, and Campbell to reply to a letter from the Director General of the E.M.S. about the rehabilitation of cardiac patients, and the Council hoped after some explanations and additions to publish the substance of this communication.
   (*d*) The Council had instructed the Secretary to write to the Registrar of the Royal College of Physicians, to express their opinion that, if any subdivisions of physicians were made in the list of consultants, cardiologists should be included; and that if societies of specialists were consulted on this and allied questions the Cardiac Society should be included among such societies.

   [The Secretary has since received a letter from the Registrar of the Royal College of Physicians reporting that this letter had come before the Standing Joint Committee of the three Royal Colleges and that it had been decided to add the Cardiac Society to the list of Societies who are willing to give advice when asked to the Standing Joint Committee of the three Royal Colleges.]

(*e*) The Council had re-appointed the Editors of the *British Heart Journal* for a second period of five years; and had decided that no change should be made in the members of the Editorial Board for another year.

7. During the afternoon discussion, the Society, on the proposal of Geoffrey Bourne, instructed the Secretary to write to the Minister of Health, the Minister of Pensions, and the Minister of Labour and National Service, stating that the Cardiac Society was willing to help, if asked to do so, in a consultative capacity or by appointing members to serve on a committee, in relation to war or to post-war problems of a cardiac nature.

Short Communications.

Potassium and the Electrocardiogram

E. P. Sharpey-Schafer

(Published in full; pp. 80 and 85)

Observations on Diphtheritic Carditis

G. Cookson reported that preliminary observations on 54 cases of diphtheria suggested that death from circulatory failure was confined to the un-immunized child. Clinical, cardiographic, and pathological investigations were made on 7 children, aged 3 to 12 years, who died between the 3rd and 56th day of the illness. Death resulted from circulatory failure except in one in whom it occurred on the 56th day from the effects of neuritis. With early death (up to the 8th day) the course was progressively downwards from the onset, with widespread hæmorrhages. Clinical signs of congestive failure were absent, but triple rhythm was present and the cardiogram was abnormal. One patient showed terminal ventricular tachycardia. With death from the 9th day onwards the condition of the throat and neck cleared up, and then, after a varying interval of spurious convalescence, signs and symptoms of congestive and peripheral failure appeared. Liver congestion was invariably present. A progressive slowing of the heart rate was characteristic of this phase. Chief cardiac signs were a diffuse precordial impulse, disappearance or lateral extension of the apex beat, and triple ryhthm. Only once did a systolic murmur appear. The blood pressure fell progressively for some days before death. Cardiography showed axis deviation, depression of the S–T segment, and conduction disturbance. The S–T depression might be found within 48 hours of the onset; it had some diagnostic value for it had not been found in controls with other acute infections. In the 2 cases with the longest course the cardiogram showed low voltage and T changes, the type of curve found in the adult.

Post-mortem, there was increased heart weight and thickening of the wall especially of the left ventricle. There were intracardiac ante-mortem thrombi in 2 cases. Histologically the striking change was muscle degeneration to the stage of necrosis in some areas. Inflammatory and reparative processes were slight. Bilateral pleural effusions were present in 2 cases. The liver showed degeneration in the 2 cases with the shortest course, and venous congestion, usually intense, in the others. A normal heart muscle was found in the case that died on the 56th day, as a result of diaphragmatic and other palsies, after recovering from severe congestive failure. This last finding supports the general, but not universal, view that when recovery from diphtheria does occur, however severe the attack may have been, no permanent cardiac lesion remains.

An Unusual Case of Paroxysmal Tachycardia

C. G. Parsons

(Published in full; p. 187)

Complete and Partial Heart Block

Maurice Campbell

(To be published in full)

Incomplete Bundle Branch Block

C. W. C. Bain

(To be published in full)

Acute Left Auricular Failure

Crighton Bramwell and Morgan Jones described two cases of mitral stenosis, with unexpected death from acute pulmonary œdema in mid-pregnancy. In both cases a severe button-hole mitral stenosis was found at autopsy but only a presystolic murmur was present during life. The maintenance of ventricular filling in mitral stenosis was discussed and it was shown that, as chronic left auricular failure develops, ventricular filling is maintained by a gradual increase of left auricular diastolic pressure, which leads to chronic pulmonary congestion. It was suggested that when severe mitral stenosis is combined with a greatly hypertrophied left auricle, as in the two cases described, ventricular filling depends largely on auricular systole. In these circumstances, if the left auricle failed suddenly, a rapid rise of auricular diastolic pressure would occur and lead to acute pulmonary œdema.

Pseudo-angina and Para-œsophageal Hernia

S. W. Patterson described pseudo-anginal symptoms in association with para-œsophageal hernia. In cases of strangulation of the herniated viscera an acute upper abdominal crisis may simulate an attack of coronary thrombosis. Less severe symptoms of cramp-like pain in the lower chest behind the sternum, and radiating through to the back, up to the throat, and sometimes to the left shoulder, may simulate angina pectoris. These symptoms tend to follow conditions bringing about increased intra-abdominal pressure, especially posture, rather than effort and emotion. In some cases, thought to be neurosis, cardiac symptoms may arise from para-œsophageal hernia.

The mechanism of these symptoms may be (*a*) vascular, strangulation, obstruction, ulceration, hæmorrhage; (*b*) from pressure on lungs and heart; (*c*) from stimulation of the vagus terminations; or (*d*) from stimulation by stretching of the muscle-sensory fibres of the phrenic, which Mathison (Mathison, G. C. M., *Rev. Neurol. Psych.*, 1912, **10,** 553) showed experimentally in dogs, cats, and rabbits caused a rise of blood pressure and increased depth of respiration.

The Electrocardiogram in Myotonia Atrophica

William Evans said he had examined the electrocardiogram in 9 cases and had found some characteristic change in all of them. The commonest was a prolongation of the P–R interval (with phases of 2:1 heart block in one case) slurring of the QRS complex, and electrical variation. Among the commonest clinical signs were a small pulse, a low blood pressure, and slurring or splitting of first heart sound, or triple rhythm depending on the degree of delayed A-V conduction. On cardioscopy the heart was small in 4 cases and enlarged in 3 where the P–R interval was much prolonged.

Trevor Cooke said that over the past six years he had made essentially similar observations in 9 cases. Thus the blood pressure tended to be low, being 100 systolic or lower in 5 cases and in none was it higher than 120. There was a tendency to bradycardia, the usual pulse rate being between 65 and 75 whilst two cases had pulse rates below 55. The heart (in 7 cases examined radiologically) was small in all. An electrocardiogram was recorded in 8, and only 2 (aged 17 and 22 years) had entirely normal tracings. One man, aged 39, with marked wasting and moderate myotonia showed almost flat tracings. Subsequent treatment showed a slight increase in voltage comparable with his general clinical improvement. At that stage, intramuscular prostigmin and adrenalin and intravenous quinine had no effect upon the cardiogram. Two further cases consistently showed curves suggesting recent coronary occlusions and the other three showed abnormal QRS complexes, low voltage, and low T waves.

Discussion on the Significance of Systolic Murmurs (*Morning Session*)

Noble Chamberlain deprecated the use of the word " functional " to indicate murmurs that were associated with non-valvular organic changes in the cardio-vascular system. He felt that the terms " significant " and " insignificant " might be helpful. *Significant* murmurs could include those systolic murmurs that arise from valvular heart disease or from regurgitation through an enlarged valve ring or from pathological dilatation of the vessel or chamber into which the blood is travelling. *Insignificant* murmurs would include those commonly described as physiological or cardio-pulmonary and those occurring as a temporary phenomenon in anæmias and fevers. In deciding whether or not a systolic murmur was significant, he felt that the pendulum had swung too far and that there was a tendency to regard all systolic murmurs as harmless.

In the case of basal systolic murmurs, he thought that the diagnosis of aortic stenosis might be possible in the presence of a harsh systolic murmur especially associated with radiological evidence

of left ventricular enlargement but without a thrill or the characteristic anacrotic pulse. Further, murmurs which become increasingly rough are more likely to be associated with organic changes.

In the case of the mitral systolic murmur, undoubtedly the most difficult, he suggested that roughness, wide conduction, and persistence and length were characteristics more often associated with organic defects than had lately been admitted. These murmurs are usually present both in the erect and recumbent postures though more in the latter, and they are not materially modified by respiration. Whilst murmurs having these characteristics did not necessarily indicate the presence of organic disease, they could not be regarded lightly, especially in children and in the presence of a rheumatic history. It was therefore very important to consider them in relationship to the radiological and electrocardiographic changes. It was common in children to find such significant murmurs becoming associated in a few years' time with other and clearer evidence of organic heart disease. On the other hand, it was freely admitted that in adults these significant characters might never be associated with other signs, though they were more likely to be found with diastolic murmurs or with cardiac enlargement than murmurs presenting insignificant qualities, namely, quietness and inconstancy or modification by posture and respiration.

Chamberlain referred to the common occurrence of a mid-sternal systolic murmur especially at such routine examination as is employed for recruits. He thought that if such a murmur was harsh, care should be taken to exclude the presence of a thrill, a radiologically globular heart, or right ventricular preponderance in the cardiogram, and that if any of these signs were present, the diagnosis of patent interventricular septum was justifiable. If the murmur occurred alone, even though rough, he felt it could be disregarded.

William Evans spoke of two varieties of mitral systolic murmurs, the one in late systole, and the murmur of mitral incompetence. The former was not uncommon; it was loud and long, and was usually best heard with the subject in the upright posture. It was not difficult to recognize because it was separated from the first heart sound by a distinct interval; indeed, the murmur was nearer to the second heart sound than to the first. The murmur assumed importance on account of the frequency with which it was regarded as evidence of mitral disease. When 40 such cases were examined clinically and by cardioscopy the heart was shown to be healthy, so that the innocent nature of the murmur had been established.

Unlike aortic incompetence, *mitral incompetence* presented no constant pattern on clinical, radiological, or pathological examinations; indeed, a systolic murmur appeared to be the only sign allotted to it, but this murmur was also frequently present in mitral stenosis, aortic incompetence, aortic stenosis, and hypertension. Two criteria might be set up to test the presence of mitral incompetence in these conditions, namely, disease and/or dilatation of the mitral valve, and enlargement of the left auricle. These were sought radiologically and at necropsy in cases where a mitral systolic murmur was associated with one of these four conditions. They were absent except in mitral stenosis. Even in mitral stenosis Evans thought that the lesser effect of mitral incompetence, admittedly present, did not merit specific mention in diagnosis, for the term mitral stenosis was a comprehensive one standing for mitral disease caused by rheumatism, showing systolic and diastolic murmurs and characteristic changes in the contour of the heart as seen radiologically, commonly giving rise to auricular fibrillation which at the start responded favourably to digitalis, and often complicated by intra-cardiac thrombosis and embolism. Further, since the presumptive diagnosis of mitral incompetence hindered precise diagnosis of heart disease, Evans asked for the disuse of the term.

The Place of Cardiology in a Co-ordinated Medical Service (*Afternoon Session*)

F. R. Fraser spoke of the hospital services.

If it is assumed that the post-war hospital scheme will be based on the division of the country into areas, each capable of providing all the normal hospital and consultant services, there will be a " key " hospital in each area and the specialists and special units for the area will normally be situated at the " key " hospital. A number of such areas will come within the sphere of influence of a medical school and its teaching hospital; and within each area there will be subsidiary hospitals and perhaps health centres that look to the " key " hospital for support and inspiration. There should be in each area a physician specially trained and experienced in the diagnosis and treatment of cardiac and circulatory disorders. He should be on the staff of the " key " hospital, and be available for consultations at the subsidiary hospitals of the area. In association with the " key " hospital, there should also be a special hospital or unit in suitable surroundings for the treatment and rehabilitation of selected children and young adults with cardiac damage resulting from rheumatism.

BRUCE PERRY spoke of the care of the rheumatic child, some of his points being the same as those made in the preliminary reports on these subjects of the committees set up by the Cardiac Society and by the Pædiatric Association.

Acute rheumatism produces such serious effects in children that it is important all cases should be brought under skilled treatment as soon as possible. Compulsory notification seems the only method of ensuring this, and should include all cases of acute rheumatism, chorea, rheumatic heart disease, and heart murmurs of doubtful significance in children. The latter need to be included (though possibly they should be referable to the clinic rather than notifiable) to differentiate the murmurs due to rheumatic heart disease from those of less significance.

The need for hospital treatment for a long period calls for special hospitals equipped with school teachers and school apparatus. Such hospitals should be of the open-air type in the country, and could sometimes be combined with those for the treatment of children with tuberculosis. It is probably desirable that the children should, in the first place, be admitted to the main children's hospital or the children's department of the main general hospital, and should be transferred from there to the special hospital to complete their treatment. The suggested cardio-rheumatic clinic should be held in the main hospital of the region, and in addition to full medical facilities including those for radiography and electrocardiography would need an almoner's department and adequate secretarial assistance to see that the necessary help was given and that home conditions were as satisfactory as possible, and that arrangements could be made for getting children up at regular intervals as needed. It would seem disadvantageous to make a break between this clinic and the clinic continuing to help these patients when they have reached adult life and needed advice as regards occupation, pregnancy, etc., and therefore a closely related clinic for adults, perhaps in the evening, would be desirable.

MAURICE CAMPBELL spoke of the place of cardiology in relationship to general medicine, and of the cardiologist to the general physician.

The advantages of the physician specially trained in heart disease are so obvious, both from the technical knowledge of X-rays and electrocardiograms and from the clinical knowledge of heart problems, that anything to be said on the other side is sometimes forgotten. Even from the point of view of the patient himself, the suspected diagnosis of heart disease may be wrong, and the problem may be a general medical one, as there are so many general diseases overlapping with cardiac problems; it is, therefore, essential that the cardiologist should be a good general physician. Apart from the necessity for an interest in psychology, one need only mention anæmia, hyperthyroidism, diabetes, reneal disease, and certain diseases of the chest presenting themselves as dyspnœa or pain, to realize the need for wide general medical knowledge. Secondly, both from the point of view of teaching and general organization of a medical service, a man who is also a general physician is more useful. The ordinary-sized hospital is not large enough to justify the appointment of a cardiologist, and only when a medical centre is large enough to need ten or twelve physicians can one devote himself almost whole-time to cardiology.

It would probably be agreed that neurology and dermatology should be the first medical specialities to be separated off, but many would think that cardiology and diseases of the chest would be the next most important to separate. Sometimes in the smaller centres these two can be combined. The separation of pædiatrics as a medical speciality, except in so far as it applies to the care of children up to 12 or 18 months, would appear to be a mistake, as medicine makes no dividing line for age, and the disease—whether of the nervous system or of the heart or of the lungs—often starts in childhood and continues into adult life.

As regards the training of the cardiologist, no one should take up this work until he had done two to five years' general medical work of registrar status after ordinary house appointments and (if it is so decided in the future) passing the examinations and holding the appointments necessary for consultant status, and after this, two to five years' training in the special problems of cardiology.

He concluded (1) that all larger centres should have a cardiac department with a physician in charge and a second physician or registrar and the necessary technical help, and (2) that no one should be recognized as a cardiologist who has not already become a recognized general consulting physician.

* * * * *

* * * * * *

Luncheon was served at St. Thomas' Hospital, by the kindness of the Governors of the Hospital. As it was not possible to arrange a formal dinner, the members met at 1 Devonshire Place, W.1, by the invitation of the Chairman and John Parkinson.

INDEX

A

Alam, G. M. (and F. H Smirk): Casual and basal blood pressure. 152 and 156.
Alkalosis, heart changes in (J. S. Lawrence and E. N. Allott). 128.
Allott, E. N. (and J. S. Lawrence): Heart changes in alkalosis. 128.
Amin, Massif (and M. Gatman, and F. H. Smirk): Casual and basal blood pressure in renal hypertension. 161.
Aneurysm, bacterial (E. Noble Chamberlain). 121.
Angina pectoris, syphilitic (Evan Jones and D. Evan Bedford). 107.
Anginal pain in myxœdema (A. A. Fitzgerald Peel). 89.
Atebrin, plasmoquin, and quinine, effects of, on the electrocardiogram (H. L. Heimann and B. G. Shapiro). 131.
Atrial and ventricular septal defect, congenital heart block with (A. A. Fitzgerald Peel). 11.
Auricular fibrillation late in the course of diphtheria (A. M. G. Campbell, P. C. Gibson, and C. R. T. Lane). 183.
Auriculo-ventricular dissociation with high ventricular rate in paroxysmal tachycardia (C. G. Parsons). 187.

B

Bacterial aneurysm (E. Noble Chamberlain). 121.
Bain, C. W. Curtis (and J. Parkinson): Common aorto-pulmonary trunk; a rare congenital defect. 97.
Basal blood pressure, casual and (G. M. Alam, M. Gatman, F. H. Smirk, and Massif Amin). 152 and 161.
Bedford, D. Evan (and Evan Jones): Syphilitic angina pectoris. 107.
Blood pressure, basal and casual (G. M. Alam, M. Gatman, Massif Amin, and F. H. Smirk). 152 and 161.
Bramwell, Crighton: Signs simulating those of mitral stenosis. 24.

C

Campbell, A. M. G. (and P. C. Gibson and C. R. T. Lane): Auricular fibrillation late in the course of diphtheria. 183.
Campbell, Maurice: Congenital complete heart block. 15.
Campbell, Maurice: Latent heart block. 163.
Campbell, Maurice: Partial heart block with dropped beats. 55.
Cardiac infarction, chest lead CR_7 in (William Evans and A. Hunter). 73.
Cardiac pain, reference of, to a phantom left arm (H. Cohen and H. Wallace-Jones). 67.
Cardiac Society of Great Britain and Ireland, Proceedings of the. 243.
Cardiac syndromes complicating diabetes and their treatment (K. Shirley Smith). 1.
Casual and basal blood pressure (G. M. Alam, F. H. Smirk, M. Gatman, and Massif Amin). 152 and 161.
Cerebral aneurysm (leaking), coarctation of the aorta, and double mitral A-V orifice (J. N. P. Davies and J. A. Fisher). 197.
Chamberlain, E. Noble: Bacterial aneurysm. 121.
Chest lead CR_7 in cardiac infarction (William Evans and Alastair Hunter). 73.
Cloake, P. C. P. (and W. T. Cooke): Extreme cardiac hypertrophy. Report of two cases with aortic hypoplasia and endocrine disorders. 139.
Coarctation of the aorta, double mitral A-V orifice, and leaking cerebral aneurysm (J. N. P. Davies and J. A. Fisher). 197.
Cohen, H. (and H. Wallace-Jones): The reference of cardiac pain to a phantom left arm. 67.
Combined ventricular strain, electrocardiographic patterns of (R. Lagendorf, M. Hurwitz, and L. M. Katz). 27.
Common aorto-pulmonary trunk: a rare congenital defect (C. W. Curtis Bain and John Parkinson). 97.
Complete heart block, congenital (Maurice Campbell). 15.
Congenital complete heart block (Maurice Campbell). 15.
Congenital defect: common aorto-pulmonary trunk (C. W. Curtis Bain and John Parkinson). 97.
Congenital defect: persistent truncus arteriosus (Robert Marshall). 194.
Congenital heart block (Maurice Campbell). 15.
Congenital heart block with atrial and ventricular septal defect (A. A. Fitzgerald Peel). 11.
Congenital heart block with dextrocardia (Duncan Leys). 8.
Cooke, W. Trevor (and A. B. Taylor): Treatment of subacute infective endocarditis with heparin and chemotherapy. 238.
Cooke, W. Trevor (and P. C. P. Cloake): Extreme cardiac hypertrophy; report of two cases with aortic hypoplasia and endocrine disorders. 139.
Cooke, W. Trevor (and P. D. White): Paroxysmal ventricular tachycardia. 33.
Coronary thrombosis, fatal, in a man aged twenty-two (Sloan Miller and W. W. Woods). 101.

D

Davies, J. N. P. (and J. A. Fisher): Coarctation of the aorta, double mitral A-V orifice, and leaking cerebral aneurysm. 197.
Dextrocardia, congenital heart block with (Duncan Leys). 8.
Diabetes, and their treatment, cardiac syndromes complicating (K. Shirley Smith). 1.
Diphtheria, auricular fibrillation late in the course of (A. M. G. Campbell, P. C. Gibson, and C. R. T. Lane). 183.

E

Effects of plasmoquin, atebrin, and quinine on the electrocardiogram (H. L. Heimann and B. G. Shapiro). 131.
Eisenmenger's complex (A. J. Glazebrook). 147.
Electrocardiographic patterns of combined ventricular strain (R. Lagendorf, M. Hurwitz, and L. M. Katz). 27.
Evans, William (and A. Hunter): Chest lead CR_7 in cardiac infarction. 73.
Evans, William: Triple heart rhythm. 205.
Extreme cardiac hypertrophy, report of two cases with aortic hypoplasia and endocrine disorders (W. T. Cooke and P. C. P. Cloake). 139.

F

Fatal coronary thrombosis in a man aged twenty-two (Sloan Miller and W. W. Woods). 101.
Fisher, J. A. (and J. N. P. Davies): Coarctation of the aorta, double mitral A-V orifice, and leaking cerebral aneurysm. 197.

G

Gatman, M. (and Massif Amin, and F. H. Smirk): Casual and basal blood pressure in renal hypertension. 161.
Gibson, P. C. (and A. M. G. Campbell and C. R. T. Lane): Auricular fibrillation late in the course of diphtheria. 183.
Glazebrook, A. J.: Eisenmenger's complex. 147.

H

Heart block, congenital complete (Maurice Campbell). 15.
Heart block, congenital, with atrial septal defect (A. A. Fitzgerald Peel). 11.
Heart block, congenital, with dextrocardia (Duncan Leys). 8.
Heart block, latent (Maurice Campbell). 163.
Heart block, partial with dropped beats (Maurice Campbell). 55.
Heart changes in alkalosis (J. Stewart Lawrence and E. N. Allott). 128.
Heimann, H. L. (and B. G. Shapiro): Effects of plasmoquin, atebrin, and quinine on the electrocardiogram. 131.
Hunter, Alastair (and William Evans): Chest lead CR_7 in cardiac infarction. 73.
Hurwitz, M. (and R. Lagendorf and L. M. Katz): Electrocardiographic patterns of combined ventricular strain. 27.
Hypertrophy, cardiac (extreme). Report of two cases with aortic hypoplasia and endocrine disorders (W. T. Cooke and P. C. P. Cloake). 139.

I

Infarction, subendocardial (R. K. Price and L. R. Janes). 134.
Infective endocarditis (subacute), treatment of with heparin and chemotherapy (W. T. Cooke and A. B. Taylor). 238.

J

Janes, L. R. (and R. K. Price): Subendocardial infarction. 134.
Jones, Evan (and D. Evan Bedford): Syphilitic angina pectoris. 107.

K

Katz, L. M. (and R. Lagendorf and M. Hurwitz): Electrocardiographic patterns of combined ventricular strain. 27.

L

Lagendorf, R. (and M. Hurwitz, and L. M. Katz). Electrocardiographic patterns of combined ventricular strain. 27.
Lane, C. R. T. (and A. M. G. Campbell and P. C. Gibson). Auricular fibrillation late in the course of diphtheria. 183.
Latent heart block (Maurice Campbell). 163.
Lawrence, J. S. (and E. N. Allott): Heart changes in alkalosis. 128.
Leys, Duncan: Congenital heart block with dextrocardia. 8.

M

Marshall, Robert: Persistent truncus arteriosus. 194.
Miller, Sloan (and W. W. Woods): Fatal coronary thrombosis in a man aged twenty-two. 101.
Mitral A-V orifice (double), coarctation of the aorta, and leaking cerebral aneurysm (J. N. P. Davies and J. A. Fisher). 197.
Mitral stenosis, signs simulating those of (Crighton Bramwell). 24.
Myxœdema, anginal pain in (A. A. Fitzgerald Peel). 89.

P

Parkinson, John (and C. W. Curtis Bain): Common aorto-pulmonary trunk: a rare congenital defect. 97.
Paroxysmal tachycardia, A-V dissociation with high ventricular rate in (C. G. Parsons). 187.
Paroxysmal tachycardia, ventricular (W. Trevor Cooke and Paul D. White). 33.
Parsons, Clifford G.: Complete A-V dissociation with high ventricular rate in paroxysmal tachycardia. 187.
Partial heart block with dropped beats (Maurice Campbell). 55.
Peel, A. A. Fitzgerald: Anginal pain in myxœdema. 89.
Peel, A. A. Fitzgerald: Congenital heart block with atrial and ventricular septal defect. 11.

Pericardial effusion, tuberculous (S. Suzman). 19.
Persistent truncus arteriosus (Robert Marshall). 194.
Phantom left arm, reference of cardiac pain to a (H. Cohen and H. Wallace-Jones). 67.
Plasmoquin, atebrin, and quinine, effects of on the electrocardiogram (H. L. Heimann and B. G. Shapiro). 131.
Potassium effects on the electrocardiogram of thyroid deficiency (E. P. Sharpey-Schafer). 85.
Potassium effects on T wave inversion in myocardial infarction and preponderance of ventricle (E. P. Sharpey-Schafer). 85.
Price, R. Kimball (and L. R. Janes): Subendocardial infarction. 134.
Proceedings of the Cardiac Society of Great Britain and Ireland. 243.

Q

Quinine, plasmoquin, and atebrin, effects of on the electrocardiogram (H. L. Heimann and B. G. Shapiro). 131.

R

Reference of cardiac pain to a phantom left arm (H. Cohen and H. Wallace-Jones). 67.

S

Shapiro, B. G. (and H. L. Heimann): Effects of plasmoquin, atebrin, and quinine on the electrocardiogram. 131.
Signs simulating those of mitral stenosis (Crighton Bramwell). 24.
Sharpey-Schafer, E. P.: Potassium effects on T wave inversion in myocardial infarction and preponderence of ventricle. 85.
Sharpey-Schafer, E. P.: Potassium effects on the electrocardiogram of thyroid deficiency. 85.
Smirk, F. H. (and G. M. Alam, Massif Amin, and M. Gatman): Casual and basal blood pressure. 152 and 161.
Smith, K. Shirley: Cardiac syndromes complicating diabetes and their treatment. 1.
Subendocardial infarction (R. Kimball Price and L. R. Janes). 134.
Suzman, S. Tuberculous pericardial effusion. 19.
Syphilitic angina pectoris (Evan Jones and D. Evan Bedford). 107.

T

T wave inversion in myocardial infarction and preponderance of ventricle, potassium effects on (E. P. Sharpey-Schafer). 85.
Taylor, A. B. (and W. T. Cooke): Treatment of subacute infective endocarditis with heparin and chemotherapy. 229.
Thyroid deficiency, potassium effects on the electrocardiogram of (E. P. Sharpey-Schafer). 85.
Treatment of subacute infective endocarditis with heparin and chemotherapy (W. T. Cooke and A. B. Taylor). 229.
Triple heart rhythm (William Evans). 205.
Truncus arteriosus, persistent (Robert Marshall). 194.
Tuberculous pericardial effusion (S. Suzman). 19.

V

Ventricular (and atrial) septal defect with congenital heart block (A. A. Fitzgerald Peel). 11
Ventricular tachycardia, paroxysmal (W. T. Cooke and P. D. White). 33.

W

Wallace-Jones, H. (and H. Cohen): The reference of cardiac pain to a phantom left arm. 67.
White, Paul D. (and W. T. Cooke): Paroxysmal ventricular tachycardia. 33.
Wood, W. W. (and S. Miller): Fatal coronary thrombosis in a man aged twenty-two. 101.

PRINTED IN GREAT BRITAIN BY WILLIAM CLOWES AND SONS, LIMITED, LONDON AND BECCLES